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     (FILE 'HOME' ENTERED AT 10:16:47 ON 16 OCT 2002)

     FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS, USPATFULL' ENTERED AT
     10:17:10 ON 16 OCT 2002
L1             3 S TETRABROMOERYTHROSIN
L2             3 DUP REM L1 (0 DUPLICATES REMOVED)
L3             3 S TETRA? (5A) BROMO? (5A) ERYTHROSIN?
L4             3 S TETRA? (5A) BROM? (5A) ERYTHROSIN?
L5            82 S BROM? (5A) ERYTHROSIN?
L6            54 S BROM? (3A) ERYTHROSIN?
L7            20 S L6 AND (ROSE BENGAL)
L8            12 DUP REM L7 (8 DUPLICATES REMOVED)

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L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:155443 BIOSIS
DOCUMENT NUMBER: BA67:35443
TITLE: LIGHT INTENSITY AS A CRITICAL PARAMETER IN THE DYE SENSITIZED PHOTO OXIDATION OF THE HOUSE FLY MUSCA-DOMESTICA.
AUTHOR(S): FONDREN J E JR; HEITZ J R
CORPORATE SOURCE: MISS. AGRIC. FOR. EXP. STN., DEP. BIOCHEM., MISS. STATE UNIV., MISSISSIPPI STATE, MISS. 39762, USA.
SOURCE: ENVIRON ENTOMOL, (1978) 7 (6), 891-894.
CODEN: EVETBX. ISSN: 0046-225X.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Light intensity is a critical variable of the dye-sensitized photooxidation reaction, and the rate of house fly, M. domestica, mortality is observed to increase with increasing light intensity. Relative toxicities were described for 6 xanthene dyes (**rose bengal**, octabromofluorescein, erythrosin B, phloxin B, eosin Y and tetrachlorofluorescein) as a function of the 3rd-order rate constant of photooxidation, k3, obtained for each dye and determined from the LT50 [median lethal time] tissue dye levels, and light intensity measurements. The ranking of these 6 xanthenes by their respective k3 values is almost identical to the ranking of the same dyes by their k2, or 2nd-order rate constant. The number of accumulated photons needed to produce 50% mortality was observed to decrease with an increase in light intensity.

AB. . . fly, M. domestica, mortality is observed to increase with increasing light intensity. Relative toxicities were described for 6 xanthene dyes (**rose bengal**, octabromofluorescein, erythrosin B, phloxin B, eosin Y and tetrachlorofluorescein) as a function of the 3rd-order rate constant of photooxidation, k3,. . .

IT Miscellaneous Descriptors
ROSE BENGAL OCTA **BROMO** FLUORESCEIN
ERYTHROSINE B PHLOXIN B EOSIN Y TETRA CHLORO FLUORESCEIN
XANTHENE DYES PHOTONS

L8 ANSWER 1 OF 12 USPATFULL
ACCESSION NUMBER: 2002:183911 USPATFULL
TITLE: Encapsulation of discrete quanta of fluorescent particles
INVENTOR(S): Chandler, Don J., Austin, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002096795	A1	20020725
APPLICATION INFO.:	US 2002-103807	A1	20020325 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-639819, filed on 17 Aug 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-149227P	19990817 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATENT ADMINSTRATOR, KATTEN MUCHIN ZAVIS ROSENMAN, 525 WEST MONROE STREET, SUITE 1600, CHICAGO, IL, 60661-3693
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 775
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides novel encapsulation compositions and methods. In particular, the invention relates to fluorescent capsule compositions, which consists of a layer of a polymer shell enclosing one or more fluorescent materials such as fluorescent microspheres and which are capable of emitting at least two distinct fluorescent signals. Also provided are methods for their preparation. The compositions and methods of this invention are useful in a variety of applications, including preparation of multiplexed arrays for industrial, chemical, immunological, and genetic manipulation and analysis especially as related but not limited to flow cytometry.

DETD . . . Naphtyl Sulphonic Acid), Dansyl NH-CH3, DAPI, Diamino Phenyl Oxydiazole (DAO), Dimethylamino-5-Sulphonic acid, Dipyrromethene boron Difluoride, Diphenyl Brilliant Flavine 7GFF, Dopamine, Eosin, **Erythrosin** ITC, Ethidium **Bromide**, Euchrysin, FIF (Formaldehyde Induced Fluorescence), Flazo Orange, Fluo 3, Fluorescamine, Fura-2, Genacryl Brilliant Red B, Genacryl Brilliant Yellow 10GF, Genacryl. . . 123, Rhodamine 5 GLD, Rhodamine 6G, Rhodamine B, Rhodamine B 200, Rhodamine B Extra, Rhodamine BB, Rhodamine BG, Rhodamine WT, **Rose Bengal**, Serotonin, Sevron Brilliant Red 2B, Sevron Brilliant Red 4G, Sevron Brilliant Red B, Sevron Orange, Sevron Yellow L, SITS (Primuline), . . .

L8 ANSWER 2 OF 12 USPATFULL
ACCESSION NUMBER: 2002:262214 USPATFULL
TITLE: Bacterial transglycosylases: assays for monitoring the activity using Lipid II substrates analogs and methods for discovering new antibiotics
INVENTOR(S): Kahne, Suzanne Walker, Princeton, NJ, United States
PATENT ASSIGNEE(S): The Trustees of Princeton University, Princeton, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6461829	B1	20021008
APPLICATION INFO.:	US 2000-518080		20000303 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-122966P	19990303 (60)

US 1999-137696P 19990604 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Leary, Louise N.
LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 44
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 1344

AB This invention provides a direct method for monitoring bacterial transglycosylase activity using labeled substrates produced by chemo-enzymatic synthesis wherein the labels are selected to permit the detection of both polymeric and non-polymeric products simultaneously, either directly or following the separation of product from starting material. The invention promotes the discovery of new antibiotics with activity against bacterial transglycosylases by a) laying the groundwork for structural analysis of purified, active transglycosylase (which permits structure-based design); and b) providing an assay that can be used to screen for inhibitors.

DETD . . . Naphthyl Sulfonic Acid), Dansyl NH--CH3 in water, DAPI, Diamino Phenyl Oxydiazole (DAO), Dimethylamino-5-Sulfonic acid, Diphenyl Brilliant Flavine 7GFF, Dopamine, Eosin, **Erythrosin** ITC, Ethidium **Bromide**, Euchrysin, FIF (Formaldehyde Induced Fluorescence), Flazo Orange, Fluo 3, Fluorescamine, Fura-2, Genacryl Brilliant Red B, Genacryl Brilliant Yellow 10GF, Genacryl. . . 123, Rhodamine 5 GLD, Rhodamine 6G, Rhodamine B, Rhodamine B 200, Rhodamine B Extra, Rhodamine BB, Rhodamine BG, Rhodamine WT, **Rose Bengal**, Serotonin, Sevron Brilliant Red 2B, Sevron Brilliant Red 4G, Sevron Brilliant Red B, Sevron Orange, Sevron Yellow L, SITS (Primuline),. . .

L8 ANSWER 3 OF 12 USPATFULL
ACCESSION NUMBER: 2001:121329 USPATFULL
TITLE: Microparticles attached to nanoparticles labeled with flourescent dye
INVENTOR(S): Chandler, Mark B., Austin, TX, United States
Chandler, Don J., Austin, TX, United States
PATENT ASSIGNEE(S): Luminex Corporation, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6268222	B1	20010731	
APPLICATION INFO.:	US 1999-234841		19990122	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-72160P	19980122 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Horlick, Kenneth R.
ASSISTANT EXAMINER: Siew, Jeffrey
LEGAL REPRESENTATIVE: Villacorta, Gilberto M.Pepper Hamilton, LLP
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel fluorescent article comprising a core or carrier particle having on its surface a plurality of smaller polymeric particles or nanoparticles, which are stained with different fluorescent dyes. When excited by a light source they are capable of giving off multiple fluorescent emissions simultaneously, which is useful for multiplexed analysis of a plurality of analytes in a sample. The coupled complex particles carrying on their surface fluorescent nanoparticles,

methods of preparing such polymer articles, and various applications and methods of using such particles are claimed.

SUMM . . . Naphtyl Sulphonic Acid), Dansyl NH-CH3, DAPI, Diamino Phenyl Oxydiazole (DAO), Dimethylamino-5-Sulphonic acid, Dipyrrometheneboron Difluoride, Diphenyl Brilliant Flavine 7GFF, Dopamine, Eosin, **Erythrosin** ITC, Ethidium **Bromide**, Euchrysin, FIF (Formaldehyde Induced Fluorescence), Flazo Orange, Fluo 3, Fluorescamine, Fura-2, Genacryl Brilliant Red B, Genacryl Brilliant Yellow 10GF, Genacryl. . . 123, Rhodamine 5 GLD, Rhodamine 6G, Rhodamine B, Rhodamine B 200, Rhodamine B Extra, Rhodamine BB, Rhodamine BG, Rhodamine WT, **Rose Bengal**, Serotonin, Sevron Brilliant Red 2B, Sevron Brilliant Red 4G, Sevron Brilliant Red B, Sevron Orange, Sevron Yellow L, SITS (Primuline),. . .

L8 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 94198357 MEDLINE
DOCUMENT NUMBER: 94198357 PubMed ID: 8148434
TITLE: Removal of biological stains from aqueous solution using a flow-through decontamination procedure.
AUTHOR: Lunn G; Klausmeyer P J; Sansone E B
CORPORATE SOURCE: Program Resources, Inc./DynCorp, Environmental Control and Research Program, NCI-Frederick Cancer Research and Development Center, Maryland 21702-1201.
SOURCE: BIOTECHNIC AND HISTOCHEMISTRY, (1994 Jan) 69 (1) 45-54. Journal code: 9107378. ISSN: 1052-0295.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940523
Last Updated on STN: 19940523
Entered Medline: 19940509

AB Chromatography columns filled with Amberlite XAD-16 were used to decontaminate, using a continuous flow-through procedure, aqueous solutions of the following biological stains: acridine orange, alcian blue 8GX, alizarin red S, azure A, azure B, brilliant blue G, brilliant blue R, Congo red, cresyl violet acetate, crystal violet, eosin B, eosin Y, **erythrosin** B, ethidium **bromide**, Giemsa stain, Janus green B, methylene blue, neutral red, nigrosin, orcein, propidium iodide, **rose Bengal**, safranine O, toluidine blue O, and trypan blue. Adsorption was most efficient for stains of lower molecular weight (< 600). Adsorption of stain increased as the flow rate decreased; column diameter had little effect on adsorption. Adsorption of stain was greatest when finely ground resin was used, but if the resin particles were too small, column clogging occurred. Limited grinding of the resin gave increased adsorption while retaining good flow characteristics. Amberlite XAD-16 saturated with methylene blue was regenerated to its initial adsorption capacity by passing methanol through the column. The technique described provides an economical, rapid means of removing stains from aqueous solution.

AB . . . A, azure B, brilliant blue G, brilliant blue R, Congo red, cresyl violet acetate, crystal violet, eosin B, eosin Y, **erythrosin** B, ethidium **bromide**, Giemsa stain, Janus green B, methylene blue, neutral red, nigrosin, orcein, propidium iodide, **rose Bengal**, safranine O, toluidine blue O, and trypan blue. Adsorption was most efficient for stains of lower molecular weight (< 600).. . .

L8 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92247921 MEDLINE
DOCUMENT NUMBER: 92247921 PubMed ID: 1725856
TITLE: Decontamination of aqueous solutions of biological stains.
AUTHOR: Lunn G; Sansone E B
CORPORATE SOURCE: Program Resources Inc., NCl-Frederick Cancer Research and

Development Center, Maryland 21702-1201.
CONTRACT NUMBER: NO1-CO-74102 (NCI)
SOURCE: BIOTECHNIC AND HISTOCHEMISTRY, (1991) 66 (6) 307-15.
Journal code: 9107378. ISSN: 1052-0295.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19960129
Entered Medline: 19920608

AB Aqueous solutions of a number of biological stains were completely decontaminated to the limit of detection using Amberlite resins. Amberlite XAD-16 was the most generally applicable resin but Amberlite XAD-2, Amberlite XAD-4, and Amberlite XAD-7 could be used to decontaminate some solutions. Solutions of acridine orange, alcian blue 8GX, alizarin red S, azure A, azure B, Congo red, cresyl violet acetate, crystal violet, eosin B, **erythrosin** B, ethidium **bromide**, Janus green B, methylene blue, neutral red, nigrosin, orcein, propidium iodide, **rose Bengal**, safranine O, toluidine blue O, and trypan blue could be completely decontaminated to the limit of detection and solutions of eosin Y and Giemsa stain were decontaminated to very low levels (less than 0.02 ppm) using Amberlite XAD-16. Reaction times varied from 10 min to 18 hr. Up to 500 ml of a 100 micrograms/ml solution could be decontaminated per gram of Amberlite XAD-16. Fourteen of the 23 stains tested were found to be mutagenic to Salmonella typhimurium. None of the completely decontaminated solutions were found to be mutagenic.

AB . . . orange, alcian blue 8GX, alizarin red S, azure A, azure B, Congo red, cresyl violet acetate, crystal violet, eosin B, **erythrosin** B, ethidium **bromide**, Janus green B, methylene blue, neutral red, nigrosin, orcein, propidium iodide, **rose Bengal**, safranine O, toluidine blue O, and trypan blue could be completely decontaminated to the limit of detection and solutions of. . .

L8 ANSWER 6 OF 12 USPATFULL
ACCESSION NUMBER: 89:27822 USPATFULL
TITLE: Supersensitization of and reduction of dark decay rate in photoconductive films
INVENTOR(S): Carolla, Donald J., St. Paul, MN, United States
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Company, St. Paul, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4820620		19890411
APPLICATION INFO.:	US 1987-115695		19871102 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1986-887074, filed on 17 Jul 1986, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goodrow, John L.
LEGAL REPRESENTATIVE: Sell, Donald M., Kirn, Walter N., Jordan, Robert H.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 656
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A photocoductive film comprising at least one photosensitive material dispersed in a resinous binder is supersensitized and the dark decay rate thereof reduced by adding an effective amount of an organic acid having at least one carboxyl functional group and at least one hydroxyl functional group to the coating mixture from which the film is formed. The organic acid is an independent component of the coating mixture and is substantially not copolymerized with the binder resin.

SUMM . . . useful for altering the spectral sensitization of, for example, zinc oxide include: azomethine dyes, cyanine dyes, fluorescein dyes, rosaniline dyes, **erythrosin** dyes, **rose bengal**, **bromophenol** blue, basic fuchsin, methyl green, methylene blue, etc. Several of these dyes are more fully described in U.S. Pat. Nos.:. . .

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L8 ANSWER 7 OF 12 USPATFULL

ACCESSION NUMBER:	84:37213 USPATFULL
TITLE:	Etchable electrophotographic long-run printing plate and method of making same
INVENTOR(S):	Bhattacharjee, Himangshu R., Rockaway, NJ, United States Hopf, Frederick R., Parsippany, NJ, United States Beeson, Karl W., Princeton, NJ, United States
PATENT ASSIGNEE(S):	Allied Corporation, Morris Township, Morris County, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4457992		19840703	
APPLICATION INFO.:	US 1983-492771		19830509	(6)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Welsh, John D.
LEGAL REPRESENTATIVE:	Hoffman, Thomas D., Fuchs, Gerhard H., Doernberg, Alan M.
NUMBER OF CLAIMS:	29
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	784

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An etchable electrophotographic printing plate comprising a coating on a surface of an electroconductive support such as grained, anodized aluminum of effective amounts of photoconductive ZnO and of a sensitizing dye dispersed in an organic resin binder comprised of about 60-90 wt. % of C.sub.2 -C.sub.4 alkenyl C.sub.2 -C.sub.8 alkanoate, about 5-30 wt. % of di(C.sub.1 -C.sub.8 alkyl) C.sub.4 -C.sub.8 alkenedionate, about 2-8 wt. % of C.sub.3 -C.sub.8 alkenoic acid or C.sub.4 -C.sub.8 alkenedioic acid, and about 0.5-5.0 wt. % of a cross-linking agent. The preferred thermally cross-linkable organic resin binder is a random copolymer of 70 wt. % vinyl acetate, 24 wt. % dibutyl maleate; 5 wt. % acrylic acid and 1 wt. % glycidyl methacrylate. The etchable printing plate of the present invention is environmentally safe, has excellent shelf life and high sensitivity to actinic radiation. A process of image-wise exposure of the etchable electrophotographic printing plate to a low-power laser combined with an environmentally-safe aqueous etchant to prepare a printing plate that provided 100,000 good quality impressions is also disclosed.

SUMM . . . that have been found to be useful for spectral sensitization of zinc oxide are cyanine dyes, fluorescein dyes, rosaniline dyes, **erythrosin** dyes, **rose bengal**, **bromophenol** blue, malachite green, crystal violet, basic fuchsin, methyl green, brilliant green, methylene blue, acridine orange, alizarin red and other dye. . .

DETD . . . the range of 350-900 nm. Sensitizing dyes can be one or more of the following dyes: sodium fluorescein, eosin dyes, **rose bengal**, malachite green, anthraquinone green, brilliant green, methylene blue, bromophenol blue, **bromocresol** purple, **bromothymol** blue, **erythrosin** dyes, and cyanine dyes. Other dye systems compatible with zinc oxide are also considered to be

within the scope of. . .

L8 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1983:221814 BIOSIS
DOCUMENT NUMBER: BA75:71814
TITLE: CHARACTERISTICS OF IODO THYRONINE TYROSYL RING DEIODINATION BY RAT CEREBRAL CORTICAL MICROSOMES.
AUTHOR(S): KAPLAN M M; VISSER T J; YASKOSKI K A; LEONARD J L
CORPORATE SOURCE: THYROID DIAGN. CENT., BRIGHAM AND WOMEN'S HOSP., 75 FRANCIS ST., BOSTON, MASS. 02115, USA.
SOURCE: ENDOCRINOLOGY, (1983) 112 (1), 35-42.
CODEN: ENDOAO. ISSN: 0013-7227.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The biochemical properties of tyrosyl ring (5-) deiodination of L-T3 and L-T4 by cerebrocortical microsomes from euthyroid rats were studied. Incubations contained radioiodinated L-T3 or L-T4 and dithiothreitol (DTT), and products were analyzed by paper chromatography. The pH maximum was 7.5 for 5-deiodination of both T3 and T4. Increasing the DTT concentration from 5 to 200 mM caused a progressive increase in the 5-deiodination rate of 2 nM T3, but at 500 mM DTT the rate decreased. When 3 DTT concentrations (5.25, 10.1, and 20.1 mM) were used, double reciprocal plots of 5-deiodination rate as a function of T3 concentration (from 0.3-40 nM) showed a sequential type kinetic pattern, with a limiting Ka of 1.7 nM L-T3. Cerebral microsomes from 4-day-old rats had an apparent Km for L-T3 similar to that of cerebrocortical microsomes from adult rats, but the neonatal tissues had a 3.5- to 10-fold higher apparent maximum velocity. At 50 mM DTT, L-T3 and L-T4 each inhibited 5-deiodination of the other. The apparent Km and Ki [inhibition constant] for L-T3 were 5.5 and 8.0 nM, respectively, the apparent Km and Ki for L-T4 were 37 and 48 nM, respectively, and the apparent maximum velocities for 5-deiodination of T3 and T4, respectively, were 134 and 144 f[femto]mol/min per mg protein. There was dose-dependent inhibition of L-T3 5-deiodination by triiodothyroacetic acid, D-T3, tetraiodothyroacetic acid, 3,5-L-diiodothyronine, 3,3'-L-diiodothyronine, iopanoic acid, **rose bengal**, L-rT3, **erythrosine**, **bromphenol** blue, and anilinonaphthalenesulfonic acid (in decreasing order of potency). There was no effect on reaction rate by addition of 3'-L-monoiodothyronine, L-thyronine, diiodothyronine, amiodarone, dicoumarol, NaI, propylthiouracil (PTU), sodium salicylate, sodium fluoride, EDTA, CaCl2 or MgCl2. The properties of the rat brain iodothyronine tyrosyl ring deiodinase differ from those of both the PTU-sensitive and PTU-insensitive pathways of 5'-deiodination in rat brain and also differ from the properties of the iodothyronine 5-deiodinase in rat liver.
AB. . . per mg protein. There was dose-dependent inhibition of L-T3 5-deiodination by triiodothyroacetic acid, D-T3, tetraiodothyroacetic acid, 3,5-L-diiodothyronine, 3,3'-L-diiodothyronine, iopanoic acid, **rose bengal**, L-rT3, **erythrosine**, **bromphenol** blue, and anilinonaphthalenesulfonic acid (in decreasing order of potency). There was no effect on reaction rate by addition of 3'-L-monoiodothyronine,. . .

L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:155443 BIOSIS
DOCUMENT NUMBER: BA67:35443
TITLE: LIGHT INTENSITY AS A CRITICAL PARAMETER IN THE DYE SENSITIZED PHOTO OXIDATION OF THE HOUSE FLY MUSCA-DOMESTICA.
AUTHOR(S): FONDREN J E JR; HEITZ J R
CORPORATE SOURCE: MISS. AGRIC. FOR. EXP. STN., DEP. BIOCHEM., MISS. STATE UNIV., MISSISSIPPI STATE, MISS. 39762, USA.
SOURCE: ENVIRON ENTOMOL, (1978) 7 (6), 891-894.
CODEN: EVETBX. ISSN: 0046-225X.

FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Light intensity is a critical variable of the dye-sensitized photooxidation reaction, and the rate of house fly, M. domestica, mortality is observed to increase with increasing light intensity. Relative toxicities were described for 6 xanthene dyes (**rose bengal**, octabromofluorescein, erythrosin B, phloxin B, eosin Y and tetrachlorofluorescein) as a function of the 3rd-order rate constant of photooxidation, k3, obtained for each dye and determined from the LT50 [median lethal time] tissue dye levels, and light intensity measurements. The ranking of these 6 xanthenes by their respective k3 values is almost identical to the ranking of the same dyes by their k2, or 2nd-order rate constant. The number of accumulated photons needed to produce 50% mortality was observed to decrease with an increase in light intensity.
AB. . . fly, M. domestica, mortality is observed to increase with increasing light intensity. Relative toxicities were described for 6 xanthene dyes (**rose bengal**, octabromofluorescein, erythrosin B, phloxin B, eosin Y and tetrachlorofluorescein) as a function of the 3rd-order rate constant of photooxidation, k3,. . .
IT Miscellaneous Descriptors
ROSE BENGAL OCTA **BROMO** FLUORESCEIN
ERYTHROSINE B PHLOXIN B EOSIN Y TETRA CHLORO FLUORESCEIN
XANTHENE DYES PHOTONS

L8 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:102381 BIOSIS
DOCUMENT NUMBER: BR17:42381
TITLE: AN INVESTIGATION OF LIGHT AS A VARIABLE PARAMETER OF DYE SENSITIZED PHOTO OXIDATION IN THE HOUSE FLY.
AUTHOR(S): FONDREN J E JR; HEITZ J R
SOURCE: J. Miss. Acad. Sci., (1978) 23 (SUPPL), 102.
CODEN: JMSSAN. ISSN: 0076-9436.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: Unavailable
IT Miscellaneous Descriptors
ABSTRACT HOUSE FLY FIRE ANT BOLL WEEVIL FACE FLY TOXICITY SUN
ROSE BENGAL OCTA **BROMO** FLUORESCEIN
ERYTHROSINE B PHLOXIN B EOSIN YELLOWISH TETRA CHLORO FLUORESCEIN MORTALITY

L8 ANSWER 11 OF 12 USPATFULL
ACCESSION NUMBER: 71:5071 USPATFULL
TITLE: PRINTING AND COATING APPARATUS
INVENTOR(S): Remer, Robert K., Evanston, IL, United States
PATENT ASSIGNEE(S): Inca Inks, Inc., Evanston, IL, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3565039		19710223
APPLICATION INFO.:	US 1969-840591		19690625 (4)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1965-455936, filed on 14 May 1965, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: McIntosh, John P.
LEGAL REPRESENTATIVE: Greist, Lockwood, Greenawalt & Dewey
NUMBER OF CLAIMS: 6
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1520
AB An apparatus for coating web and object surfaces wherein a formulation including a coating component dispersed in a solvent vehicle is deposited onto the web or object surface which is then subjected to improved solvent release means for facilitating vaporization of the

solvent constituent in the formulation and/or polymerization and crosslinking within the coating component while on the web or object surface.

DETD The cadmium sulfide, Hycar 1432 and trichloroethylene are thoroughly mixed together. The **Rose Bengal** is then added with constant stirring to insure a uniform distribution throughout the mixture. This coating formulation can be applied. . .

DETD . . . include vinyl pyrrololidone, gelatin, polyvinyl alcohol, dialdehyde starch, and protein polymers. Other coal tar dyestuffs which can be employed include **bromophenyl** blue, pinacyanol, and **erythrosin**. Other light sensitive chemicals which can be used include copper-cadminum sulfide, iodoform, anthracine, and 2, 2, 1Azobis-isobuty acrylonitrile. Catalysts which. . .

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:572199 CAPLUS
DOCUMENT NUMBER: 77:172199
TITLE: Ternary silver complexes
AUTHOR(S): Shkrobot, E. P.; Lukashenkova, N. V.; Tolmacheva, N. S.; Rodman, G. I.
CORPORATE SOURCE: USSR
SOURCE: Sb. Nauch. Tr., Nauch.-Issled. Inst. Tsvet. Metal. (1971), No. 34, 22-32
From: Ref. Zh., Met. 1972, Abstr. No. 3K100
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB From Ref. Zh., Met. 1972, Abstr. No. 3K100. The reaction of Ag with eosine, bromopyrogallol red, pyrogallol red, **Rose Bengal**, **erythrosine**, fluorescein, **bromophenol** blue, or bromophenol red, in combination with 0-phenanthroline or 2,2'-bipyridine to form a ternary complex was investigated. The detn. of Ag as the ternary complex after sepn. by ion exchange is described.

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ST silver detn; eosine silver detn; bromopyrogallol red silver detn; pyrogallol red silver detn; **Rose Bengal** silver detn; erythrosine silver detn; fluorescein silver detn; bromophenol blue red silver detn; phenanthroline silver detn; bipyridine silver detn

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L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:155443 BIOSIS
DOCUMENT NUMBER: BA67:35443
TITLE: LIGHT INTENSITY AS A CRITICAL PARAMETER IN THE DYE SENSITIZED PHOTO OXIDATION OF THE HOUSE FLY MUSCA-DOMESTICA.
AUTHOR(S): FONDREN J E JR; HEITZ J R
CORPORATE SOURCE: MISS. AGRIC. FOR. EXP. STN., DEP. BIOCHEM., MISS. STATE UNIV., MISSISSIPPI STATE, MISS. 39762, USA.
SOURCE: ENVIRON ENTOMOL, (1978) 7 (6), 891-894.
CODEN: EVETBX. ISSN: 0046-225X.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Light intensity is a critical variable of the dye-sensitized photooxidation reaction, and the rate of house fly, M. domestica, mortality is observed to increase with increasing light intensity. Relative toxicities were described for 6 xanthene dyes (**rose bengal**, octabromofluorescein, erythrosin B, phloxin B, eosin Y and

tetrachlorofluorescein) as a function of the 3rd-order rate constant of photooxidation, k3, obtained for each dye and determined from the LT50 [median lethal time] tissue dye levels, and light intensity measurements. The ranking of these 6 xanthenes by their respective k3 values is almost identical to the ranking of the same dyes by their k2, or 2nd-order rate constant. The number of accumulated photons needed to produce 50% mortality was observed to decrease with an increase in light intensity.

=> d l8 ibib ab kwic9
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ti

L8 ANSWER 1 OF 12 USPATFULL
TI Encapsulation of discrete quanta of fluorescent particles

=> d l8 ibib ab kwic 9

L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:155443 BIOSIS
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IT Miscellaneous Descriptors
ROSE BENGAL OCTA **BROMO** FLUORESCEIN **ERYTHROSINE** B PHLOXIN B EOSIN Y TETRA CHLORO FLUORESCEIN XANTHENE DYES PHOTONS

WEST

End of Result Set

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L2: Entry 1 of 1 File: USPT Jul 14, 1998

DOCUMENT-IDENTIFIER: US 5780052 A
TITLE: Compositions and methods useful for inhibiting cell death and for delivering an agent into a cell

US Patent No. (1):
5780052

Brief Summary Text (17):
Preferably, the antineoplastic agent is selected from the group consisting of cytotoxic agents, toxins, radiosensitizing compounds, alpha-emitting radionuclides, beta-emitting radionuclides, antiproliferative agents and genes (for cytokines such as IL-2 and TNF). Preferably, the cells are killed with radiation, chemotherapy or immunotherapy.

Detailed Description Text (55):
For imaging purposes, any of the well-known medical radionuclides can be used. Suitable radionuclides include Tc-99 m, I-123, I-125, In-111, In-113 m, Ga-67, or other suitable gamma-emitters.

Detailed Description Text (87):
Modern techniques for nonsurgical treatment of cancer include both clinical and experimental techniques involving chemotherapy, radiation therapy, a combination of chemotherapy and radiation therapy, and immunotherapy. In each instance, the object of the therapy is to kill the malignant cells. Antineoplastic agents presently or potentially useful in such therapy include cytotoxic drugs, biological response modifiers, radiosensitizing compounds, toxins, and radionuclides.

Detailed Description Text (91):
One diagnostic procedure of the present invention involves diagnosing sites of necrosis in an organ or tissue. This procedure utilizes immunoliposomes specific for intracellular antigens and containing a diagnostic agent, e.g., a detectable molecule such as an imaging agent. One example of such an agent is a gamma-emitting radionuclide of the type previously discussed. The radionuclide may be attached to a convenient carrier molecule, such as a chelating polymer. The radionuclide-containing immunoliposome is injected (preferably intravenously) into a patient suspected of containing an organ or tissue that is undergoing cell death; for example, a patient who has received chemotherapy, radiation therapy, or both. This procedure is preferably carried out at least one or two days after the initiation of the therapy, in order to permit resultant necrosis of the neoplastic tissue to advance to a sufficient point that reasonable numbers of necrotic cells are present. Between 30 minutes and 3 days following administration of the labeled antibody, an appropriate scintigraphic imaging technique is employed to image the label that is localized in necrotic tissue. Suitable imaging techniques include gamma cameras and SPECT (single photon emission computed tomography) techniques.

Detailed Description Text (92):
One alternative imaging technique is radiographic imaging. In this technique, immunoliposomes specific for intracellular antigen that has been labeled with a radiopaque material is injected a suitable time after initiation of chemotherapy or radiation therapy. After the antibody has localized at the areas of necrotic tissue, radiographic imaging is performed. Other suitable techniques include CAT (computed

axial tomography) scans, fluoroscopy and conventional X-ray imaging.

Detailed Description Text (95):
In the augmentation approach, tumor necrosis is initiated by any conventional technique, such as chemotherapy, immunotherapy, radiation therapy, or the like.

Detailed Description Text (125):
The following sets of images are recorded in each animal: in vivo during the experiment, of the whole heart ex vivo and as 1-cm ring slices cut perpendicular to the long axis of the left ventricle. Scintigraphic images are obtained using a gamma camera (Ohio-Nuclear 100, Solon, Ohio) equipped with a medium-energy collimator. The pulse height analyzer are set at center lines of 247 and 159 keV with 20% windows for .sup.111 In and .sup.123 I radioisotopes, respectively. Concurrent with antibody injections, sequential 1-min acquisition images are recorded for a total of 8 min. The excised hearts are imaged whole and as 1-cm thick slices for both isotopes. Background images are also collected at each isotope setting for identical acquisition time. The background corrected and peak-normalized sets of images are recorded on floppy disks and the experiment number, treatment and sequence of injection of .sup.111 In-and .sup.123 I-labeled antimyosin antibody are blinded. The infarct size is assessed twice individually by three observers. Semiautomatic planimetry is performed with a Technicare 560 computer (Technicare Corp., Solon, Ohio) to determine the infarct size as the number of pixels, as previously described (Khaw et al., J. Nucl. Med. 28:76-82, 1987). The pixel size is calibrated, and the absolute volume of infarcted tissue is determined (area.times.slice thickness). This value, multiplied by the specific gravity of myocardium (1.05), is used to determine the weight of the infarcted tissue in grams (Ostrzega et al., Am. Heart J. 117:444-452, 1989). The percent infarct relative to the ventricular mass is then calculated for the statistical analysis.

L2: Entry 3 of 4 File: USPT Jan 5, 1993

DOCUMENT-IDENTIFIER: US 5177073 A
TITLE: Therapeutic compositions derived from photoactive compounds

INVENTOR (1):
Gulliya; Kirpal S.

Drawing Description Text (2):
FIG. 1 shows where matrix support can couple to carboxyl containing unactivated 3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymethyl amino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl]benzothiazolium chloride as indicated by four vertical lines. The matrix support is a sepharose having free amino groups.

Drawing Description Text (3):
FIG. 2 shows where matrix support can couple to carboxyl containing unactivated 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl]benzothiazolium bromide as indicated by two vertical lines. The matrix support is a sepharose having free amino groups .

Detailed Description Text (13):
The photoactive compounds are generally compounds, such as dyes, having one or more chromophores and capable of absorbing light energy. The term "chromophore" refers to portions of a molecule that are fundamentally responsible for the electronic transition. These photoactive compounds can be cationic, anionic, zwitterionic, or neutral. They comprise chemical classes and their respective derivatives, including, but are not limited to: acridine, anthraquinone; azine; azo, which comprises disazo, monoazo, pyrazolones, and triazo; azomethine; carbocyanine; coumarins; diphenylmethane; flaven; flavone; flavylium salts; indigoid; methylidyne; nitro; nitroso; polymethylidyne; natural dyes such as porphyrin derivatives; psoralens; quinonimines; sulfide; sulfur; thiazole; toluidine; triphenylmethane; xanthene; and others. Their derivatives may contain functional groups, such as hydroxyl, carboxyl, thiol, or amino group, all of which are capable of forming chemical bonds through coupling reactions.

Detailed Description Text (56):
N,N'-Bis(2-ethyl-1,3-dioxolane)kryptocyanine (EDKC) can be prepared by methods such as those disclosed by F. M. Hammer, J. Chem. Soc., 2796-2804 (1927), and the disclosure of which is incorporated by reference herein. In brief, 1-(2-ethylene-1,3-dioxolane)-4-methylquinolinium bromide (0.66 g, 2 mmol) and dry pyridine (6 ml) are stirred at 110.degree. C. under a nitrogen atmosphere until solution occurred. To this is to be added triethylorthoformate (0.75 g, 5 mmol) and stirring is to continue for 2 hr. The deep cyan colored solution is to be cooled and poured into rapidly stirred ethyl ether (200 ml). The crude product can be isolated by filtration and purified by medium-pressure column chromatography (Woelm 32-63 silica gel, methylene chloride/methanol). The fractions that are homogeneous by thin layer chromatography analysis (silica gel, 5% methanol/methylene chloride) are to be combined. A solution of the resultant EDKC in a complete medium can be irradiated with laser light for about 10 minutes around the wavelength region from about 650 nm to about 725 nm maintained at about 1 to 2 watts.

Detailed Description Text (103):
Synthesis of

3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymethyl amino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium chloride. A mixture of 4.8 g (20.2 mmol) of 5-amino-2-methylbenzothiazole dibydrochloride and 7.65 g (55.1 mmol) of 2-bromacetic acid were refluxed in 35 ml of cyclobexane for 15 hours. After cooling to room temperature, solution was evaporated to dryness (yield 4 g) and was used crude in the next step. About 3 g (9.5 mmol) of 2-methylbenzothiazolediocetic acid derivative obtained from the previous reaction was refluxed with 1.1 g (8.3 mmol) of 1,3,3-trimethoxypropene in 10 ml of pyridine for 3 hours. After cooling to room temperature, 300 ml of 3M HCl was added to precipitate approximately 2 g of product as reddish-brown solid. Carbocyanine was collected by filtration, dissolved in 40 ml of 0.5M NaOH and recrystallized. (Yield 1.5 g)

Detailed Description Text (105):
Synthesis of 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl]benzothiazolium bromide. A mixture of 2.54 ml (2.98 g, 20.0 mmol) of 2-methylbenzothiazole and 3.1 ml (3.78 g, 25.0 mmol) of 1-bramopentane were refluxed in 35 ml of cyclohexane overnight (12 hours). Cyclohexane was evaporated under reduced pressure to leave a yellow liquid from which a small amount of low melting crystalline material was obtained. The remaining residue was used for the subsequent reaction with trimethoxypropene without further purification. (Yield about 12 g). Approximately 11 g (38 mmol) of (N-2'-methylbenzothiazolium) acetic acid bromide salt prepared from the previous reaction was combined with 3.96 g (30 mmol) of 1,3,3-trimethoxypropene in 30 ml of dry pyridine and the whole mixture was refluxed for 4 hours. Upon the completion of the reaction, dark slurry was brought to room temperature, acidified with 140 ml of 3N HCl and refrigerated overnight. Filtration of this solution yielded a deep blue solid which was isolated, dried, weighed, and recrystallized from 160 ml of 0.5M sodium hydroxide.

Detailed Description Text (107):
Cytotoxicity of Carbocyanines Coupled to Matrix Supports. Carbocyanine dyes 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide and 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide were covalently coupled, or immobilized, to AH-Sepharose 4B beads (40 to 210 um diameter, Pharmacia, LKB Biotechnology Products, Piscataway, N.J.) by the manufacturer's recommended procedure. Briefly, 2 mg of a carbocyanine dye in 50% ethanol H.sub.2 O at pH 4.5, was allowed to react with 1 g (dry weight) of swollen beads in the presence of 0.1M of N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride (Pharamacia). The mixture was mixed in an end-over end shaker for 24 hours at 4.degree. C. in the dark. Afterward, the uncoupled dye was removed by exhaustive washing with 50% ethanol: H.sub.2 O until free dye could not be detected spectrophotometrically. The resultant therapeutic compositions, namely, the immobilized carbocyanines, were stored in the dark at 4.degree. C. The amount of dye coupled to beads was determined by a standard curve for each dye.

Detailed Description Text (108):
Concentration of 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide=5.times.10.sup.-7 M/bead

Detailed Description Text (109):
Concentration of 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide=1.times.10.sup.-7 M/bead In this study, the cell surface was shown to be a target for the action of photoactive carbocyanines. Human promyelocytic leukemia cells (HL-60 cell line) were exposed to 10.sup.-3 M of carbocyanine dye coupled to sepharose beads. In one set of experiments, the mixture of cells and beads was exposed to fluorescent light, cells were washed and allowed to incubate overnight at 37.degree. C. in a CO.sub.2 atmosphere of 5% CO.sub.2 in air. After overnight incubation, the viability of cells was determined by trypan blue dye exclusion. In these experiments, greater than 60% of cells were killed upon exposure to light compared to the untreated cells or cells exposed to native sepharose beads alone. In another set of experiments, native beads and beads covalently coupled with carbocyanine were exposed to light first, then washed and mixed with leukemic cells. After overnight incubation, beads and cells

were separated by filtration through a Whatman filter (size 3) that allowed the cells to pass through but retained the sepharose beads due to their large size. The viability of cells was determined by trypan blue dye exclusion method. The beads recovered from these experiments were reused and mixed with fresh HL-60 cells, and the process was repeated. In these experiments, it was observed that light-exposed (pre-activated) beads were capable of at least six "re-uses," or sequential killings, of HL-60 cells with some losses due to interim manipulations. Thus, the therapeutic composition of immobilized carbocyanine killed the HL-60 cells while native sepharose beads were not toxic to these tumor cells. See Table 16.

Detailed Description Text (112):
Cytotoxicity of 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium Bromide Coupled to an Antibody. Carbocyanine 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta- 1,3-dien-1-yl] benzothiazolium bromide was covalently coupled to anti-cytokeratin monoclonal antibody (Dako Corporation, Santa Barbara, Calif.). This antibody reacts with the Ca. 54 kd protein corresponding to cytokeratin 8 of the Moll catalog. It reacts with all non-squamous epithelium). The antibody and carbocyanines were covalently coupled by mixing the 5 mg of antibody with 5 mg of carbocyanine in 10% ethanol: H.sub.2 O in the presence of 0.1M of N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide hydrochloride. The unreacted dye was separated from the antibody on a desalting column. The recovered antibody was used in phosphate buffered saline at pH 7.4.

Detailed Description Paragraph Table (16):
TABLE 16 CYTOTOXICITY OF PRE-ACTIVATED THERAPEUTIC COMPOSITION CONTAINING CARBOCYANINES COUPLED TO SEPHAROSE BEADS % Kill of HL-60 Tumor Cells Control 4.5 Native Beads 5.0 Unactivated Carbocyanine 1* 15.8 Unactivated Carbocyanine 2** 10.3 Carbocyanine 1* 1st Use 63 2nd Use -- 3rd Use 77 4th Use 86.3 5th Use 27.7 6th Use 36.8 7th Use 31.2

*3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymeth lamino-2-benzothiazolinylidene) methylbuta1,3-dien-1-yl]benzothiazolium chloride
**3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta1,3-dien-1-yl]benzothiazolium bromide

Detailed Description Paragraph Table (17):
TABLE 17 CYTOTOXICITY OF 3-CARBOXYMETHYL-2-[4-(3- CARBOXYMETHYL-2-BENZOTHIAZOLINYLIDENE) METHYLBUTA-1,3-DIEN-1-YL]BENZOTHIAZOLIUM BROMIDE COUPLED TO AN ANTIBODY Presence of Antibody on the Cells as Determined by FITC Labelled % Cell Kill 2nd Antibody Uncoupled Antibody (Control) 5 + Pre-activated Uncoupled Antibody 5 + (Control) Unactivated Carbocyanine Coupled 15 + to Antibody Pre-activated Carbocyanine 50 + Coupled to Antibody

CLAIMS:

6. A therapeutic composition in accordance with claim 1 wherein said photoactive compound is selected from the group consisting of 3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymethyl amino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium chloride and 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide.

12. A therapeutic composition in accordance with claim 7 wherein said photoactive compound is selected from the group consisting of 3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymethyl amino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium chloride and 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide.

20. A therapeutic composition in accordance with claim 18 wherein said carbocyanine compound is selected from the group consisting of 3-carboxymethyl-5-carboxymethylamino-2-[4-(3-carboxymethyl-5-carboxymethyl

amino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium chloride and 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide.

23. A therapeutic composition in accordance with claim 21 wherein said photoactive compound is 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide.

24. A therapeutic composition in accordance with claim 23, wherein said 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide is covalently coupled to said antibody through amide linkages.

29. A therapeutic composition in accordance with claim 25 wherein said photoactive compound is selected from the group consisting of 3-carboxymethyl-5-carboxymethylamino-2[4-(3-carboxymethyl-5-carboxymethyla mino-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium chloride and 3-carboxymethyl-2-[4-(3-carboxymethyl-2-benzothiazolinylidene) methylbuta-1,3-dien-1-yl] benzothiazolium bromide.

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     FILE 'WPIDS' ENTERED AT 14:07:00 ON 13 SEP 1999
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BROMOERYTHROS
L2          125 S ERYTHROSIN#
L3          349 S L1 OR L2
L4         1290 S XANTHENE#
L5          286 S L4 (L) (HALOGEN? OR BROMO OR IODO)
L6          630 S L5 OR L3
L7          153 S RADIOSENS?
L8         5875 S IONI? (5A) RADIAT?
L9         8008 S IMAG? (5A) CONTRAS?
L10        2942 S CONTRAST? (5A) (MEDIUM OR AGENT?)
L11          45 S CAT SCAN
L12       38770 S X RAY
L13           8 S L6 AND (L7 OR L8 OR L9 OR L10 OR L11 OR L12)
L14           0 S CHEMICAL PARTION?
L15           0 S L6 AND L14
L16           3 S CHEMICAL PARTITION?
L17           0 S L6 AND L14
L18           0 S L6 AND L16
L19           0 S PARTITION? AND L6
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L21           2 S L6 AND L20
L22           1 S TOMOGRAPHY AND L6
L23       52969 S TISSUE#
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L27  ANSWER 1 OF 13  WPIDS COPYRIGHT 1999   DERWENT INFORMATION LTD
AN   1997-132381 [12]   WPIDS
DNC  C1997-042719
TI   Fluorogenic substrates for diagnosis and photo-dynamic therapy of tumours
     - contain masking gps. removable by cell enzymes, partic. those in
tumour,
     give higher ratio of active cpd. in tumour-healthy cells.
DC   B02 B04 D16 J04
IN   BAGLIONI, P; BOTTIROLI, G; CROCE, A C; MONICI, M
PA   (CNDR) CONSIGLIO NAZ DELLE RICERCHE
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         W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KE KG KP KR KZ
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            TR TT UA UG US UZ VN
     AU 9667351    A  19970218 (199723)
     WO 9703697    A3 19970410 (199729)
     EP 839051     A1 19980506 (199822)  EN
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     IT 1275571    B  19970806 (199825)
ADT  WO 9703697 A2 WO 1996-EP3201 19960719; AU 9667351 A AU 1996-67351
     19960719; WO 9703697 A3 WO 1996-EP3201 19960719; EP 839051 A1 EP
     1996-927559 19960719, WO 1996-EP3201 19960719; IT 1275571 B IT
1995-MI1560
     19950719
FDT  AU 9667351 A Based on WO 9703697; EP 839051 A1 Based on WO 9703697
PRAI IT 1995-MI1560   19950719
AB   WO   9703697 A UPAB: 19970320
     Fluorogenic substrates (FS), capable of fluorescence emission and
     photosensitisation activity on enzyme transformation, and suitable for
     diagnosis and photodynamic therapy of tumours, comprise fluorescent
     substances with high yield of photosensitisation activity, modified
     chemically by introducing a gp. which quenches these properties, but is
     removable by enzyme activity in the tumour cells, with restoration of the
     fluorescence and photosensitisation properties.
          The FS consist of Rose Bengal acetate, phosphate,
     monobutyrate or dibutyrate; haematoporphyrin or protoporphyrin IX
     monoacetate, diacetate and phosphate; phthalocyanine monoacetate,
     diacetate, and phosphate, or hypericin polyacetate or polyphosphate. The
     FS include derivs. of xanthene, porphyrins, phthalocyanines, chlorines or
     perylenequinonoid pigments. Quenching gps. include acetate, sulphate,
     phosphate, dibutyryl ester,  galactopyranoside, glucuronide or
     acetamido-deoxyglucopyranoside.
```

USE - The substrates are applied in all sectors of diagnosis and photodynamic therapy in oncology. Partic. reference is to tumours in cavities, in conjunction with fibre optic systems and endoscopy, and to topical tumours. Possible applications are in haematic pathologies and purging of bone marrow for autologous transplant. Systemic admin. is as an isotonic saline soln. or a **liposome** suspension. Topical admin. is from solns. favouring absorption and penetration of the FS, e.g., as a soln. in 50% i-PrOH contg. ca. 2% azone, a penetrant agent. Amts. are 1-10 mg/kg.

ADVANTAGE - The enzyme removing the quenching gp. in the FS is one expressed in greater quantity in the tumour cells, causing preferential accumulation of the active substance in tumour rather than healthy cells.This results in better distinction in outlining the tumour mass, and less damage to healthy cells.

Dwg.0/6

L27 ANSWER 2 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
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DNC C1995-151317
TI Use of coloured NMR or **X-ray contrast agents**, or ultrasound **contrast agents** - for prepn. of diagnostic **agents** for visual marking of bodily tissues.
DC B05
IN FRITZSCH, T; HEYWANG-KOEBRUNNER, S; SPECK, U; WEITSCHIES, W
PA (SCHD) SCHERING AG
CYC 20
PI WO 9520981 A1 19950810 (199544)* DE 23p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP US
DE 4403789 A1 19950810 (199544) 5p
EP 742724 A1 19961120 (199651) DE
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 09508397 W 19970826 (199744) 18p
ADT WO 9520981 A1 WO 1995-EP123 19950113; DE 4403789 A1 DE 1994-4403789 19940203; EP 742724 A1 EP 1995-906937 19950113, WO 1995-EP123 19950113; JP 09508397 W JP 1995-520342 19950113, WO 1995-EP123 19950113
FDT EP 742724 A1 Based on WO 9520981; JP 09508397 W Based on WO 9520981
PRAI DE 1994-4403789 19940203
AB WO 9520981 A UPAB: 19951109
Use of coloured NMR **contrast agents**, coloured **X-ray contrast agents**, or dye-contg. ultrasound **contrast agents**, for prepn. of diagnostic **agents** for visual labelling of bodily tissues, is new.

PREFERRED MATERIALS - The coloured NMR **contrast agent** is a metalloporphyrin, a magnetic iron oxide cpd., nitrogen oxide and/or melanin. The **X-ray contrast agent** is **Rose Bengal, erythrosin** or tetrachlorotetraiodo-fluorescein (**Rose Bengal** lactone).The ultrasound **contrast agent** comprises a coat of a biologically degradable polymer (esp. a polylactide-glycolide or polycyanoacrylate) and a core contg. a gas (and opt a dye).

USE - The diagnostic agents may be used in diagnosis of, e.g., tumours (such as mammary carcinoma) using magnetic resonance **tomography, X-ray** or ultrasound techniquesosage of **contrast agent** is 0.1-100 mumol/ml of injected soln.

ADVANTAGE - The diagnostic agent is well tolerated, remains in the desired area for a sufficient length of time, is detachable both visually and radiologically, and is injectable through long, thin cannulae.

Dwg.0/0

L27 ANSWER 3 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1995-275290 [36] WPIDS
CR 1999-189704 [16]
DNC C1995-124819
TI Inhibiting lymphocyte proliferation with transition metal complexes - esp. of vanadium, tungsten and molybdenum complexed with oxo and peroxo gps.; useful for treating leukaemia or lymphoma(s).
DC B05
IN SCHIEVEN, G L
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 21
PI WO 9520390 A1 19950803 (199536)* EN 166p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP MX US
EP 735880 A1 19961009 (199645) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5565491 A 19961015 (199647) 36p
US 5583242 A 19961210 (199704) 29p
JP 09508392 W 19970826 (199744) 141p
US 5693627 A 19971202 (199803) 31p
MX 9603094 A1 19970301 (199820)
US 5846998 A 19981208 (199905)
ADT WO 9520390 A1 WO 1995-US1234 19950130; EP 735880 A1 EP 1995-909397 19950130, WO 1995-US1234 19950130; US 5565491 A US 1994-189330 19940131; US 5583242 A Div ex US 1994-189330 19940131, US 1995-450342 19950525; JP 09508392 W JP 1995-520240 19950130, WO 1995-US1234 19950130; US 5693627 A Div ex US 1994-189330 19940131, US 1995-450401 19950525; MX 9603094 A1 MX 1996-3094 19960730; US 5846998 A CIP of US 1994-189330 19940131, WO 1995-US1234 19950130, US 1996-669499 19960618
FDT EP 735880 A1 Based on WO 9520390; JP 09508392 W Based on WO 9520390; US 5693627 A Div ex US 5565491; US 5846998 A CIP of US 5565491, Based on WO 9520390
PRAI US 1994-189330 19940131; US 1995-450342 19950525; US 1995-450401 19950525; US 1996-669499 19960618
AB WO 9520390 A UPAB: 19990424

Proliferation of T cells, B cells or their malignantly transformed derivs.

is inhibited by treatment with a coordinate covalent complex (CCC) comprising: (i) a metal ion selected from Mo(VI), W(VI), or V (V) ion; (ii) an oxo gp. covalently bonded to the metal ion; (iii) opt. at least 1 peroxo gp. coordinate-covalently bonded to the metal ion; and (iv) at least 1 organic moiety (I) coordinate-covalently bound to the metal through at least 1 N-or O-contg. functional gp. able to donate electrons to the coordinate-covalent bond. (CCC) has sufficient affinity for the active site of phosphotyrosine phosphatase (PTP) to inhibit the activity of this enzyme. In a variant, (I) is boned through an N, O or As contg. gp. able to donate electrons and (CCC) contains 1 or 2 peroxo gps.

occupying 2 sites in the coordination sphere of the metal ion. (CCC) are new cpds. where: (a) the metal ion is not V(V); and (b) the complex has affinity for the PTP active site at least to that of bis(maltolato)oxovanadium (IV) (BMLOV).

USE - The CCC are used to treat leukaemia or lymphoma (derived from opt. transformed T or B cells or myeloid cells), partic. in conjunction with **ionising radiation**, where a synergistic effect is achieved and apoptosis is induced. They can also be used to prevent class-switching of antibody producing cells to reduce IgE formation (treatment of allergy), and to induce tyrosine phosphorylation in (transformed) T and B cells (as a result of PTP inhibition and/or tyrosine kinase activation). The CCC can be used to suppress growth of tumour cells overexpressing a tyrosine kinase (esp. HER1-4 or Src) or requiring PTP for growth and/or survival, opt. in conjunction with a therapeutic agent and to activate tyrosine kinases of the 352/60 family (all claimed). Further uses include control of B cell proliferation to treat autoimmune disease and transplant rejection, treatment of protozoal infection, studies on B cells to determine susceptibility to radiation and chemicals etc., and purging of bone marrow for autologous transplants. The CCC are admin. to provide 1-100 mu M in the blood and/or tissue, partic. given orally or by injection.

ADVANTAGE - Treatment with (A) is specific for lymphocytes and does not induce neutropaenia (A) are active against some tumours resistant to other drugs.

Dwg.17/21

L27 ANSWER 4 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-226552 [28] WPIDS
DNC C1993-100839
TI New vectored drug **delivery** system - comprises organ-specific, non-antibody vectoring reagent, linking agent and therapeutically-active agent.
DC B07
IN SHARMA, Y P
PA (SHAR-I) SHARMA Y P
CYC 1
PI US 5225182 A 19930706 (199328)* 14p
ADT US 5225182 A US 1991-786044 19911031
PRAI US 1991-786044 19911031
AB US 5225182 A UPAB: 19931116

A new compsn. for the vectored selective **delivery** of a therapeutically-active agent to a desired mammalian target system, organ, tissue or cell comprises a conjugate composed of an organ-specific, non-antibody vectoring reagent (I) selective for the organ, tissue or cell, a linking entity (II), comprising a cephaloplastin cpd., coupled to it and a therapeutically-active agent (III) coupled to the linking agent, the conjugate being capable of releasing (III) with retention of its therapeutic activity to the organ, tissue or cell. (I) and (II) are coupled by passive adsorption and/or covalent bonding. (II) and (III) are also coupled by passive adsorption and/or covalent bonding.

(I) may be e.g. aggregated albumin, albumin colloid, disofenin, eitdronate, phosphate, sulphur colloid, succimer, glucoheptonate, pentetrate, gallium citrate, **rose bengal**, white blood cells, orthoiodohippurate, selenomethionine or thallous chloride.

Substances other than cephaloplastin cpds. can also be used as linking agents, e.g. typed red blood cells, Hogeman factor, proconvertin, lectins and thymosin.

USE/ADVANTAGE - Using the compsn., functional (III) is localised rapidly and directly in the desired organ or tissue of choice, so that a reduced dose of drug can be administered and side effects are minimised. The method is used partic. in the treatment of cancer.

Dwg.0/0

L27 ANSWER 5 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-076187 [09] WPIDS
DNC C1993-033566
TI Persistent pi-system free radicals as **contrast agents** - used in magnetic resonance **imaging**, are stable, have long half lives and long relaxation times.
DC B05 P31
IN ANDERSSON, S; RISE, F; WIKSTROM, H; WISTRAND, L; GOLMAN, K; WIKSTROEM, H
PA (NYCO-N) NYCOMED INNOVATION AB; (NYCO-N) NYCOMED IMAGING AS
CYC 22
PI WO 9302711 A1 19930218 (199309)* EN 137p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: AU CA FI JP NO US
AU 9224238 A 19930302 (199326)
NO 9400410 A 19940208 (199417)
FI 9400566 A 19940311 (199420)
JP 07502724 W 19950323 (199520)
EP 662004 A1 19950712 (199532) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
US 5435991 A 19950725 (199535) 42p
AU 668691 B 19960516 (199627)
US 5700448 A 19971223 (199806) 43p
EP 662004 B1 19980318 (199815) EN 103p
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
DE 69224850 E 19980423 (199822)
ES 2114566 T3 19980601 (199829)
ADT WO 9302711 A1 WO 1992-EP1793 19920806; AU 9224238 A AU 1992-24238 19920806; NO 9400410 A WO 1992-EP1793 19920806, NO 1994-410 19940208; FI 9400566 A WO 1992-EP1793 19920806, FI 1994-566 19940208; JP 07502724 W WO 1992-EP1793 19920806, JP 1993-503287 19920806; EP 662004 A1 EP 1992-916836 19920806, WO 1992-EP1793 19920806; US 5435991 A WO 1992-EP1793 19920806, US 1994-190045 19940318; AU 668691 B AU 1992-24238 19920806; US 5700448 A Div ex WO 1992-EP1783 19920806, Div ex US 1994-190045 19940318, US 1995-415662 19950403; EP 662004 B1 EP 1992-916836 19920806, WO 1992-EP1793 19920806; DE 69224850 E DE 1992-624850 19920806, EP 1992-916836 19920806, WO 1992-EP1793 19920806; ES 2114566 T3 EP 1992-916836 19920806
FDT AU 9224238 A Based on WO 9302711; JP 07502724 W Based on WO 9302711; EP 662004 A1 Based on WO 9302711; US 5435991 A Based on WO 9302711; AU 668691 B Previous Publ. AU 9224238, Based on WO 9302711; US 5700448 A Div ex US 5435991; EP 662004 B1 Based on WO 9302711; DE 69224850 E Based on EP 662004, Based on WO 9302711; ES 2114566 T3 Based on EP 662004
PRAI GB 1991-17418 19910812; GB 1991-17211 19910809
AB WO 9302711 A UPAB: 19950810
Use of a persistent pi-system free radical, other than a chloranil semiquinone anion or trityl radical, for mfr. of a **contrast**

medium for use in magnetic resonance imaging (MRI), in which the electron delocalising pi-system comprises at least one homo- or heterocyclic ring, is new.

Also claimed are certain radicals and their precursors.

The radical has an inherent linewidth in its esr spectrum of less than 500 mG, and contains a mesomeric structural gp. X1-(C=C)n-X2 (a) X1 = O, S, N, C, or quaternary N radical; X2 = an atom or gp. capable of participating in the pi-bond system; and n = a positive integer. Examples are given as phenoxy, indolyl, indolizinyl, acridinyl, dihydropyranyl, thioaminyl, bipyridyl, enolate, timoprazolyl, cinnolyl, koelsch, semiquinone, quinolinoxy, diphenylpicryl, galvinoxyl, dibenzoyl indigo, fluorenyl, diarylamino, **rose bengal**, indoloxy or dicyanoquinone radicals, and phenoxy diradical.

USE - The radicals are used in OMRI (Overhauser MRI) for diagnostic purpose in human and veterinary medicine. They are stable at physiological pH, have long half lives, long relaxation times, good relaxivity and the water-soluble ones are partic. important for these purposes. They may also be coupled to other molecules, e.g., lipophilic moieties, for improving relaxivity, or to macromolecules, e.g. polymers, proteins, polypeptides, polysaccharides, and polyethyleneimines. The macromole may be tissue specific e.g. an antibody

Dwg.0/0

Dwg.0/0

L27 ANSWER 6 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-284937 [39] WPIDS
DNN N1991-217870 DNC C1991-123490
TI IMmunoassay method - by reacting delayed fluorescence or phosphorescence-labelled antibody or antigen particles with antigen or antibody and irradiating.
DC A96 B04 S03
PA (MITU) MITSUBISHI KASEI CORP
CYC 1
PI JP 03188374 A 19910816 (199139)* 8p
JP 2893772 B2 19990524 (199926) 7p
ADT JP 03188374 A JP 1989-329093 19891219; JP 2893772 B2 JP 1989-329093 19891219
FDT JP 2893772 B2 Previous Publ. JP 03188374
PRAI JP 1989-329093 19891219
AB JP 03188374 A UPAB: 19930928
A method for immunoassay of antigen or antibody in sample comprises (a) supporting (i) a dye emitting delayed fluorescence or phosphorescence and (ii) antigen or antibody on insoluble carrier particles of 0.01-1 microns particle size to form dye-labelled particles, (b) reacting the dye-labelled particles with a sample liq. contg. corresp. antibody or antigen to cause agglutination reaction of the particles by antigen-antibody reaction and (c) irradiating a polarised exciting light to the reaction liq. and measuring the degree of emission polarisation.

The dye emitting delayed fluorescence or phosphorescence has a long fluorescent or phosphorescent life (pref. 100 micro sec.-10 m sec). The dye emitting delayed flourescence is e.g. an dye such as eosin, metallic porphyrin cpd. or metal chelating agent e.g. Eu, Tb or Sm, etc. The dye emitting phosphorescence is e.g. aq. soln. of eosin or **erythrosin** (2',4',5',7'-tetraiodo-fluorescein). The insoluble carrier particles are

e.g. an organic high polymer latex of polystyrene, silica, **liposome**, erythrocyte, golden colloid, etc. The antibody is e.g. IgG, pepsin, etc. The antigen is e.g. protein, polypeptide, steroid, polysaccharide, lipid, etc.

USE/ADVANTAGE - The invention relates to emission polarisation immunoassay using insoluble carrier particles. Not only low mol. antigen such as drug, hormone, etc. but also high mol. antigens such as a protein can be determined with simplicity and accuracy of latex agglutination, and the homogeneous reaction system and sensitivity of fluorescent polarisation immunoassay (FPIA). @(8pp Dwg.No.0/0)

L27 ANSWER 7 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-101849 [14] WPIDS
CR 1991-177867 [24]; 1992-415456 [50]; 1997-502270 [46]
DNC C1991-043637
TI Poly aromatic polymers as glucosamino glycan mimics - for use as anticoagulants in treatment of thrombosis, bone metabolism and neuronal disorders.
DC A96 B04 B07
IN BENSASSON, S; CHANG, M; EILAT, D; KREGAN, J R
PA (RORE) RORER INT HOLDINGS INC; (RORE) RORER INT HOLDINGS INC
CYC 15
PI WO 9103226 A 19910321 (199114)* 30p
RW: BE CH DE DK ES FR GB IT LI LU NL SE
W: AU CA JP
PRAI US 1989-393873 19890814
AB WO 9103226 A UPAB: 19990723
The polyaromatic polymer has a mol. wt. of 2000-20000 daltons contains 1-10 opt. substd. rings on each monomeric unit and is essentially free from monomer. There are pref. 3-10 rings each contg. at least one substit. selected from NRR1, -N:R, OR, :O, NO2, COOR, halogen, SO2-OR, SO2NHR, OSO2-OR or R (R1 is alkyl, H or opt. substd. phenyl and R is 1-12C alkyl).

Specific monomer units include aluminon, anazolene, Na, Eosine I bluish, Eosine yellowish, **Erythrosine**, Evans blue, Fast green, FCF, Fuchsin(e) acid, iodophthalein Na, methyl blue, **Rose Bengal**, Sulphobromo-phthalein Na, Suramin Na, Trypan blue, Trypan red, Rosaniline Cl, crystal violet, methyl green, Coomassie blue, basic Fuchsin, Malachite green, Brilliant green, Aniline blue, Brilliant cresyl blue, Safranin O, ethyl violet, Pararosaniline acetate and methyl violet. They have the formula (I) where a, b, c are 0 or 1, m is 5-20, dotted lines are opt. double, R is H or alkyl, R1 is H or opt. substd. Ph, X, Y, Z are -NRR1 etc. as above.

USE/ADVANTAGE - The polymer is **delivered** orally and is absorbed into the bloodstream through the gastrointestinal tract or has anticoagulant properties and mimics the activity of glycosaminoglycans. The polymer may be for treatment of neuronal disorders.
Dwg.0/0

L27 ANSWER 8 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-361245 [48] WPIDS
CR 1990-274555 [36]
DNC C1990-156953
TI Inhibition of viral replication in cells - using xanthene or thiazine

dyes, for selectively inactivating HIV.
DC B02
IN FLOYD, R A; SCHINAZI, R F
PA (OKLA-N) OKLAHOMA MEDICAL RES FOUND; (SCHI-I) SCHINAZI R F; (OKLA-N) OKLAHOMA MED RES FOUND; (OKLA-N) OKLAHOMA MED RES FO
CYC 16
PI WO 9013296 A 19901115 (199048)* 46p
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: CA JP
EP 471794 A 19920226 (199209)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04507403 W 19921224 (199306) 12p
ES 2032742 T1 19930301 (199321)
EP 471794 A4 19920506 (199521)
JP 07119173 B2 19951220 (199604) 12p
JP 08151327 A 19960611 (199633) 14p
EP 471794 B1 19961002 (199644) EN 17p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69028775 E 19961107 (199650)
US 5571666 A 19961105 (199650) 10p
ES 2032742 T3 19970201 (199712)
CA 2055463 C 19970930 (199801)
JP 2700126 B2 19980119 (199808) 14p
US 5827644 A 19981027 (199850)
ADT EP 471794 A EP 1990-909103 19900511; JP 04507403 W JP 1990-508726 19900511, WO 1990-US2659 19900511; ES 2032742 T1 EP 1990-909103 19900511; EP 471794 A4 EP 1990-909103 ; JP 07119173 B2 JP 1990-508726 19900511, WO 1990-US2659 19900511; JP 08151327 A Div ex JP 1990-508726 19900511, JP 1995-122801 19900511; EP 471794 B1 EP 1990-909103 19900511, WO 1990-US2659 19900511; DE 69028775 E DE 1990-628775 19900511, EP 1990-909103 19900511, WO 1990-US2659 19900511; US 5571666 A CIP of US 1988-264088 19881028, Cont of US 1989-350383 19890511, Cont of US 1990-632606 19901224, Cont of US 1991-758228 19910909, Cont of US 1993-29984 19930312, US 1994-251624 19940531; ES 2032742 T3 EP 1990-909103
19900511; CA 2055463 C CA 1990-2055463 19900511; JP 2700126 B2 Div ex JP 1990-508726 19900511, JP 1995-122801 19900511; US 5827644 A CIP of US 1988-264088 19881028, Cont of US 1989-350383 19890511, Cont of US 1990-632606 19901224, Cont of US 1991-758228 19910909, Cont of US 1993-29984 19930312, Cont of US 1994-251624 19940531, US 1996-707992 19960712
FDT JP 04507403 W Based on WO 9013296; ES 2032742 T1 Based on EP 471794; JP 07119173 B2 Based on JP 04507403, Based on WO 9013296; EP 471794 B1 Based on WO 9013296; DE 69028775 E Based on EP 471794, Based on WO 9013296; US 5571666 A CIP of US 4950665; ES 2032742 T3 Based on EP 471794; JP 2700126 B2 Previous Publ. JP 08151327; US 5827644 A CIP of US 4950665, Cont of US 5571666
PRAI US 1989-389007 19890803; US 1989-350383 19890511; WO 1990-US2659 19900511; US 1988-264088 19881028; US 1990-632606 19901224; US 1991-758228 19910909; US 1993-29984 19930312; US 1994-251624 19940531; US 1996-707992 19960712
AB WO 9013296 A UPAB: 19961219
Viral replication in cells is inhibited with xanthene or thiazine dyes (I).

Pref dyes are methylene blue (Ia), eosin Y (Ib) and **rose bengal** (Ic). These may be used in vitro at a concn. above 0.2 mM, or in vivo at an intracellular concn. of 0.0001-0.01 mM or a blood concn.

of 0.02-0.2 mM. For use in vivo, (I) may be administered orally, intravenously or as controlled-release polymer implants or **liposome** formulations, opt. together with antibiotics, antiinflammatory agents, antifungal agents or other antiviral agents. Their activity may be enhanced by simultaneous exposure of the blood capillaries to light through the skin.

USE/ADVANTAGE - (I) may be used to inhibit replication of viruses, esp. HIV and HSV, in vitro or in vivo. @(46pp Dwg.No.0/1)

L27 ANSWER 9 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1989-209359 [29] WPIDS
DNN N1989-159584 DNC C1989-092775
TI heat-sensitive recording material prepn. - by coating microcapsules contg.
colourless agent and aq. dispersion of organic basic cpd. in water insol. solvent, onto substrate etc..
DC A89 E23 E24 G05 P75
PA (FUJF) FUJI PHOTO FILM CO LTD
CYC 5
PI JP 01145190 A 19890607 (198929)* 15p
GB 2213280 A 19890809 (198932)
US 4929411 A 19900529 (199025)
GB 2213280 B 19920102 (199201)
JP 06104385 B2 19941221 (199504) 19p
ADT JP 01145190 A JP 1987-301561 19871201; GB 2213280 A GB 1988-27937 19881130; US 4929411 A US 1988-278320 19881201; JP 06104385 B2 JP 1987-301561 19871201
FDT JP 06104385 B2 Based on JP 01145190
PRAI JP 1987-301561 19871201
AB JP 01145190 A UPAB: 19930923
A heat-sensitive recording material is made by coating a mixt. of (a) microcapsules contq. colourless or light-coloured colouring agent and (b) an aq. dispersion of an organic baseic cpd. as a colour developing agent dissolved in a water insol. solvent, onto a substrate and drying.

Pref. the substrate is transparent. Typically the thickness of the substrate is 20-200 microns (50-100 microns). The colouring agent is, e.g.
of formula (I), and the organic basic cpd. is, e.g. cpd. (IV). The wall material of the microcapsule is, e.q., polyurethane, polyurea, polyester, polycarbonate, gelatin, Pval, etc.

USE/ADVANTAGE - Used for facsimiles, thermal printers, etc. and si suitable for over head projector sheets. The material improves transparency of the recording layer and **contrast** of **image**.

L27 ANSWER 10 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1986-079228 [12] WPIDS
DNN N1986-057871 DNC C1986-034115
TI Forming storable thermally stable image - by irradiating spiro-pyran cpd. with UV rays to form image with ring-opened colour former, then adding metal salt and leuco dye.
DC A89 E13 E24 G06 P83 T03 W04
PA (SONY) SONY CORP
CYC 1
PI JP 61028939 A 19860208 (198612)* 4p
JP 05080656 B 19931109 (199347) 5p
ADT JP 61028939 A JP 1984-150174 19840719; JP 05080656 B JP 1984-150174

19840719
FDT JP 05080656 B Based on JP 61028939
PRAI JP 1984-150174 19840719
AB JP 61028939 A UPAB: 19930922
Image-forming comprises irradiating (A) spiropyran cpd. of formula (I) as a photosensitive cpd. with UV rays to form an image with (A1) a ring-opened colour former, adding (B) a metal salt which produces a stable cpd. with (A1) and adding (C) leuco dye to form colour with (B). In (I), X is O or S; R1 is 1-20C alkyl; R2, R3, R4 and R5 are H, 1-5C alkyl, 1-5C alkoxy, **halogen**, nitro or dimethylamino; R6, R7 and R8 are H, 1-5C alkyl, 1-5C alkoxy or **halogen**.

Specifically, cpd. (B) is e.g., chloride, nitrate or sulphate of Fe(III), Ag(I), Mn(VIII) or Cr(VI). Dye (C) is e.g., thiazine series, triphenylmethane series, **xanthene** series. The molar ratio of (A), (B) and to (C) is 1:0.1-1:0.1-1. The method is carried out e.g., as follows: Cpd. (A) is dispersed in a polymer layer made of e.g., PVA or polyacrylamide, and the polymer layer is irradiated with UV rays to form desired image. The polymer layer is treated with (B) and subsequently with (C) to obtain the objective image.

USE/ADVANTAGE - The method forms image which is stable to heat and has a good storage stability. The band of light-absorption wavelength at the dark portion of image can be changed by selecting (C). The brightness of the image is inverted to the spiropyran **image** and the **contrast** of the brightness can be increased, compared with that of the spiropyran image.
0/2

L27 ANSWER 11 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1979-25003B [13] WPIDS
TI Electrophotographic photosensitive material - for **images** having high density and excellent **contrast**.
DC A89 E14 G08 P84 S06
PA (RICO) RICOH KK
CYC 1
PI JP 54024636 A 19790224 (197913)*
PRAI JP 1977-89165 19770727
AB JP 54024636 A UPAB: 19930901
An electrographic photoreceptor comprises (A) a conductive support and (B) a photoconductive layer consisting of (a) a photoconductive substance and (b) resin, and contains >=1 of (C) cpds. of formula (I) and (II).

In the formulae, R is OH, CH3, COOH, COOM, where M is alkali metal; M2 is a bivalent metal of Ca, Mg, Ni, Mn or Zn.

The photosensitive material has improved sensitivity and pre-exposing characteristics and thus provides **images** having high density and excellent **contrast**. In an example, a soln. for forming a photoconductive layer was prepd. by mixing 300 g. of Zn oxide, 125 g. of toluene soln. contg. 40% of acrylic resin, 20 g. of methanol, 0.15 g. of **Rose Bengal** and 330 g. of toluene in a ball mill. To the soln. was added 0.9 g. of cpd. (I; R = OH). The soln. was applied on a support made of an Al-deposited polyester film and dried to give a photoconductive layer of 20-30 mu thick.

L27 ANSWER 12 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1975-21583W [13] WPIDS
TI **X-ray** sensitive electrophotographic sheets - photoconductor layers contain one or more phosphors.
DC G08
PA (FUJI) ROTTE CO LTD
CYC 1
PI JP 49090938 A 19740830 (197513)*
PRAI JP 1973-457 19721229
AB JP 49090938 A UPAB: 19930831
One or more types of phosphors are included in the photoconductor layers to give **X-ray** sensitive electrophotog. plates. The inclusion of the phosphors int he photoconductor layer increases the **X-ray** sensitivity of the plate more efficiently than use of sep. phosphor plate. In an example, photoconductive ZnO (Sazex 4000) 100, Cu-activated ZnS 20-60, **Rose bengal** 0.0.01, Acrylase MM2002 (an acrylic resin from Fujikura Chem. Co.) 20-60 g were kneaded with 100 cm3 of PhMe and the mixts. were coated on elec. conductive paper substrates to give **X-ray** sensitive electrophotog. sheets whose **X-ray** sensitivities were is approx. 3 times those of electrophotog. sheets without ZnSiCu phosphors.

L27 ANSWER 13 OF 13 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1966-20435F [00] WPIDS
TI **Erythrosine** b radiopaque agent fr 3820m provided.
DC B00
PA (CNRS) CENTRE NAT DE LA RECHERCHE
CYC 3
PI BE 665986 A (196800)*
FR 3820 M (196801)
GB 1058516 A (196801)
PRAI BE 1965-665986 19650625
AB BE 665986 A UPAB: 19930831
Medicament containing **erythrosine** B (I), which may contain radio-iodine.
As radiopaque agent for use in the pancreatic region and, if desired, in the biliary and lymphatic vessels.
Experiments in the rat and cat show that after i.v. injection, (I) concentrates slowly in the pancreatic juice and forms a valuable **contrast agent** after ca. 5 hr. Before this time, it rapidly serves the same purpose for the biliary vessels.
In the cat, a dose of 1 g. in 10 ml. aq. soln. gives a max. concn. in the pancreatic juice of 0.1% and 0.04 g in 2 ml. soln. gives a concn. of 0.02%.
As a soln. containing 0.5 g/l. in physiol. saline for i.v. use.

L28 ANSWER 1 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1997-374107 [35] WPIDS
DNN N1997-310533 DNC C1997-120731
TI Conjugates containing compound capable of fluorescing, linker and protein

- are capable of distinguishing between healthy and unhealthy **tissue** and are used in imaging of e.g. tumours.

DC B04 S03
IN KAUS, M; MAIER-BORST, W; SCHRENK, H; SINN, H; STEHLE, G; WUNDER, A
PA (DEKR-N) DEUT KREBSFORSCHUNGSZENTRUM; (DKFZ-N) DKFZ DEUT KREBSFORSCHUNGSZENTRUM STIFTUN
CYC 20
PI DE 19602295 A1 19970724 (199735)* 5p
WO 9726920 A2 19970731 (199736) DE 9p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
WO 9726920 A3 19971211 (199816)
EP 877631 A2 19981118 (199850) DE
R: AT BE CH DE DK ES FR GB IT LI NL SE
ADT DE 19602295 A1 DE 1996-19602295 19960123; WO 9726920 A2 WO 1997-DE166 19970123; WO 9726920 A3 WO 1997-DE166 19970123; EP 877631 A2 EP 1997-907031 19970123, WO 1997-DE166 19970123
FDT EP 877631 A2 Based on WO 9726920
PRAI DE 1996-19602295 19960123
AB DE 19602295 A UPAB: 19970828
Conjugate comprises: (i) a compound capable of fluorescing (I); (ii) a linker; and (iii) a protein.

(I) is preferably a fluorescence dye, especially a xanthine dye such as fluorescein, aminofluorescein, **erythrosine**, aminoerythrosin, yellow eosin, yellow aminoeosin, or a derivative or analogue of these. (II) has a photodynamic activity and the conjugate may contain several of these compounds. The protein is not foreign to the body and is especially albumin. The linker is cyanuric chloride. The conjugates may be prepared by covalent linkage of components (i), (ii) and (iii).

USE - The conjugates are capable of discerning between healthy and unhealthy **tissue** (claimed). They become enriched in unhealthy **tissue**, especially tumour **tissue** (e.g. oesophageal tumour **tissue**) and neovascular **tissue** in the corneal region. The presence of the conjugates in these **tissues** may be detected using e.g. an ultraviolet lamp.

ADVANTAGE - The conjugates have half-lives suitable for imaging of **tissue**.

Dwg.0/2

L28 ANSWER 2 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1995-164315 [22] WPIDS
DNN N1995-128838 DNC C1995-075883
TI Basic gas detecting tape, unaffected by acidic gases - comprises **tissue** paper support, fluorescein dye, strongly acidic organic acid and moisture-retaining agent.
DC E19 E24 E35 J04 S03
IN NAKANO, N
PA (RIKE-N) RIKEN KEIKI CO LTD; (RIKE-N) RIKEN KEIKI KK
CYC 2
PI JP 07083911 A 19950331 (199522)* 4p
CA 2132413 A 19950314 (199524)
ADT JP 07083911 A JP 1993-278938 19930913; CA 2132413 A CA 1994-2132413 19940913
PRAI JP 1993-278938 19930913
AB JP 07083911 A UPAB: 19950609
Basic gas detecting tape consists of a fluorescein dye(s) a strongly acidic organic acid(s) and a moisture-retaining agent(s) held in a

tissue paper support.
Pref. the dye is one or a mixt. of rose benzal, froxin, **erythrosin**, eosin, yellowish and **eosin bluish**. Pref. the acid is one or a mixt. of p-toluene sulphonic, naphthalene sulphonic and benzene sulphonic acids. Pref. the moisture-retaining agent is a higher alcohol(s).
ADVANTAGE - The tape can detect ammonia and amine gases at a level as low as 100 ppb, allows prolonged measurement under exposed conditions and does not deteriorate during long storage.
Dwg.0/2

L28 ANSWER 3 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1994-074358 [09] WPIDS
CR 1996-076838 [08]
DNN N1994-058101 DNC C1994-033835
TI Examination of biological samples - using visualisation dye to facilitate retrieval of sample and positioning for sectioning.
DC B04 D22 J04 S03
IN CAMIENER, G W
PA (CAMI-I) CAMIENER G W
CYC 1
PI US 5290706 A 19940301 (199409)* 4p
ADT US 5290706 A US 1992-974071 19921110
PRAI US 1992-974071 19921110
AB US 5290706 A UPAB: 19960305
Prepn. of a biological sample for examination comprises (a) adding a gross biological sample contg. biological material selected from **tissue** and organs to a preservative medium which contains a dye that colours the gross sample in a manner in which the gross sample is visually identifiable for retrieval from among other contents of the medium and does not interfere with subsequent sectioning and staining of the gross sample for microscopic examination, (b) identifying and retrieving the gross sample from the medium based on the resulting colour differentiation, (c) sectioning the gross sample to obtain an examination sample, and (d) staining the examination sample.
The preservative medium may comprise glyoxal, HCHO or glutaraldehyde.
The dye may be e.g. **erythrosine**, erioglaucine, basic violet 3, tartrazine, amaranth, azocarmine, brilliant blue, bromocresol green, bromothymol blue, carmosine, crystal violet, indigo carmine, pararosaniline, ponceau red or sunset yellow.
USE/ADVANTAGE - The method is used with biological samples such as biopsy **tissues**, faecal samples contg. parasites and discrete organs and **tissues** such as lymph nodes. The visualisation dye stains the biological sample so as to make it easy to retrieve and easy to position in paraffin blocks for sectioning.
Dwg.0/0
Dwg.0/0

L28 ANSWER 4 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1992-079795 [10] WPIDS
DNC C1992-036911
TI Adhesive for sepd. **tissues** or prosthetic materials - comprising natural or synthetic peptide and component which forms matrix sol. or gel.

DC A96 B04 D22 G03
IN BASS, L S; EATON, A M; LIBUTTI, S K
PA (BASS-I) BASS L S; (EATO-I) EATON A M; (LIBU-I) LIBUTTI S K; (UYCO) UNIV COLUMBIA NEW YORK
CYC 22
PI WO 9202238 A 19920220 (199210)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU BR CA FI JP KP NO
AU 9184979 A 19920302 (199224)
US 5209776 A 19930511 (199320) 10p
EP 542880 A1 19930526 (199321) EN 38p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
US 5292362 A 19940308 (199410) 13p
JP 06507376 W 19940825 (199438) 14p
EP 542880 A4 19930728 (199527)
ADT AU 9184979 A AU 1991-84979 19910723, WO 1991-US5186 19910723; US 5209776 A
US 1990-560069 19900727; EP 542880 A1 EP 1991-915440 19910723, WO 1991-US5186 19910723; US 5292362 A CIP of US 1990-560069 19900727, US 1991-727607 19910709; JP 06507376 W JP 1991-514745 19910723, WO 1991-US5186 19910723; EP 542880 A4 EP 1991-915440
FDT AU 9184979 A Based on WO 9202238; EP 542880 A1 Based on WO 9202238; US 5292362 A CIP of US 5209776; JP 06507376 W Based on WO 9202238
PRAI US 1991-727607 19910709; US 1990-560069 19900727
AB WO 9202238 A UPAB: 19970723
A compsn. for bonding sepd. **tissues** together or for coating **tissues** or prosthetic materials is claimed comprising: (a) at least one first component (I) selected from natural or synthetic peptides, modified, crosslinked, cleaved or shortened variants or derivs. and (b) at least one second component (II), which is different from (I), adapted to support (I) to form a matrix, sol or gel with (I).

(I) may be, e.g., albumin, alpha-globulins, beta-globulins, gamma-globulins, transthyretin, fibrinogen, thrombin, collagen, elastin, keratin, fibroin, fibrin or fibronectin. (II) may be, e.g., hyaluronic acid, chondroitin sulphate, dermatan sulphate, keratan sulphate, heparin, heparan sulphate, collagen, fructose, dextrans, agarose, alginic acid, pectins, methylcellulose, hydroxycellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, CMC, glycerine, mannitol, sorbitol, polyvinylalcohol or polyethylene glycol. The compsn. may also contain a chromophore, e.g., indocyanine green, fluorescein, **rose bengal**, gentian violet or methylene blue.

USE/ADVANTAGE - The compsn. provides a **tissue** bond having high tensile strength elasticity, deformability, water tightness, viscosity and adhesivity for a large variety of surgical procedures. The compsn. can also be used to coat implantable devices to enhance their strength and resistance to fluids, to seal pores in the weave of the material and to reduce thrombogenicity. @(38pp Dwg.No.0/0)bi

L28 ANSWER 5 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-309962 [42] WPIDS
DNN N1991-237663 DNC C1991-134203
TI Permanently occluding arteries by inducing thrombosis - by **rose bengal** injection with laser irradiation at specific site, for arterio-vascular malformation of nervous system, etc..
DC B02 P34

IN WATSON, B D
PA (WATS-I) WATSON B D
CYC 1
PI US 5053006 A 19911001 (199142)*
ADT US 5053006 A US 1990-503130 19900402
PRAI US 1988-183046 19880419; US 1990-503130 19900402
AB US 5053006 A UPAB: 19930928
Arteries having a dia. at least 21 microns are permanent by occluded by (1) infusing **rose bengal** dye (I) into the bloodstream then (2) irradiating an individual artery with a laser light of wavelength which excites (I). The light beam is focussed to maximise overlap of its cross-sectional intensity profile with the distribution of (I) bound to arterial endothelium so that (I) attached to the luminal surface absorbs light, initiating a reaction which causes photochemical injury to the arterial endothelium at the point of (I) - laser light interaction.

Also new is a similar process using **erythrosin** B (II) as the dye.

USE/ADVANTAGE - The (I)-photosensitised endothelial surface is thrombogenic, so platelet adhesion and aggregation occur, causing complete occlusion of the artery. The method does not damage adjacent **tissue** and (I) is more efficient than Na fluorescem previously suggested as photosensitiser (quantum efficiency of singlet O2 prodn. 76% vs. 3%). The method is esp. useful for occluding very fragile (e.g. thin-walled, high-flow feeder) arteries on the underside of the nidus of an arteriovascular malformation of the nervous system, but also in ophthalmic surgery (diabetic retinopathy), for treating skin tumours and to control bleeding in the liver.
0/0

L28 ANSWER 6 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-157701 [22] WPIDS
DNC C1991-068065
TI New antiinflammatory 5-hydroxy-2-furanone derivs. - also have immuno suppressant and anti-proliferative activity, and modify calcium homeostasis.
DC B03
IN GARST, M E; SYAGE, E T
PA (ALLR) ALLERGAN INC; (GARS-I) GARST M E
CYC 20
PI EP 429287 A 19910529 (199122)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
AU 9066623 A 19910523 (199128)
JP 03170476 A 19910724 (199136)
CA 2027863 A 19910521 (199144)
US 5112853 A 19920512 (199222) 13p
EP 429287 A3 19920212 (199323)
AU 639041 B 19930715 (199335)
US 5258400 A 19931102 (199345) 12p
AU 9338491 A 19930930 (199347)
AU 655882 B 19950112 (199509)
ADT EP 429287 A EP 1990-312591 19901120; JP 03170476 A JP 1990-317639 19901120; US 5112853 A Cont of US 1989-439733 19891120, US 1991-709550 19910603; EP 429287 A3 EP 1990-312591 19901120; AU 639041 B AU 1990-66623 19901114; US 5258400 A Cont of US 1989-439733 19891120, Div ex US 1991-709550 19910603, US 1992-872776 19920423; AU 9338491 A AU 1993-38491

19930510, Div ex AU 1990-66623 ; AU 655882 B AU 1993-38491 19930510, Div ex AU 1990-66623

FDT AU 639041 B Previous Publ. AU 9066623; US 5258400 A Div ex US 5112853; AU 655882 B Previous Publ. AU 9338491

PRAI US 1989-439733 19891120

AB EP 429287 A UPAB: 19931115

New 2-furanone cpds. of formula (I) are claimed. R1 = 1-17C alkyl or alkenyl, carbocyclic aryl-(1-17C alkyl or alkenyl), heteroaryl-(1-12C alkyl or alkenyl), cyclohexyl or cyclohexyl-(1-17C alkyl or alkenyl). The alkenyl gps. have 1-5 unconjugated double bonds; X = (a) or (b), and R1 is linked to X by bond a. R2 = H or 1-4C alkyl; R3 = H or 1-17C alkanoyl.

2 Cpds. are specifically claimed, i.e., 4-(3,6-dihydro-6-hydroxy-5-(3-phenyl propyl)-2H-pyran-2yl)- and 4-(5-(6-benzo(b)-thien-2-yl)-hexyl)-3,6-dihydro- 6-hydroxy-2H-pyran-2-yl)- 5-hydroxy-2(5H)-furanone. Daily dose is 0.05-100 mg/kg.

USE/ADVANTAGE - Treating inflammatory conditions (claimed). (I) also have immunosuppressant and antiproliferative activity. Therefore useful to treat rheumatoid or osteo-arthritis, rheumatic carditis, allergic diseases, bronchial asthma, myasthenia gravis, ocular and dermal inflammatory diseases etc., and preventing organ and **tissue** transplant rejection. (I) also modify Ca homeostasis. Modification could be used in the treatment of Parkinson's or Alzheimer's disease, hypertension, cardiac infarction, atherosclerosis, ulcers, diarrhoea, etc., and neoplasia or psoriasis. @(21pp Dwg.No.0/0)@

0/0

L28 ANSWER 7 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD

AN 1990-046497 [07] WPIDS

DNC C1990-020240

TI Pharmaceutical compsns. contg. poly aromatic cpds. - useful for **tissue** redistribution of bioactive peptide(s) and proteins normally bound to glycosamino glycan(s).

DC B05

IN EILAT, D; SHMUEL, B S

PA (HADA-N) HADASSAH MEDICAL ORGANIZATION

CYC 13

PI EP 354818 A 19900214 (199007)* EN 9p

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

ADT EP 354818 A EP 1989-308214 19890814

PRAI IL 1988-87444 19880812

AB EP 354818 A UPAB: 19930928

A pharmaceutical compsn. for affecting **tissue** redistribution of bioactive peptides and proteins normally bound to glycosaminoglycans, and for mimicking the action of glycosaminoglycans in biological interactions, comprises a therapeutically effective amt. of an aromatic cpd. contg. 2-10 aromatic rings, electronegative substits. and at least 2 of the aromatic rings, and also contg. negatively charged residues on at least two of the rings.

Also claimed is the aromatic cpd. as active ingredient in the pharmaceutical compsn.

The cpd. has mol.wt. less than 1000 and is a deriv. of triphenylmethane and is selected from Aluminon halogenated 1 sulphonated or sulphonated-halogenated Aluminon, Anazolene Sodium, Eosine 1 Bluish, Eosine yellowish, **Erythrosine**, Evans blue, Fast green FCF,

Fuchsine acid, Iodophthalein Sodium methyl blue, **rose Bengal**, suramin Sodium, Trypan blue and Trypan Red.

USE/ADVANTAGE - The compsns. are useful, for removal of cationic proteins from glomerular basement membrane or connective **tissues** thus preventing local damage; modulation of LPL, in e.g. Cardiovascular diseases; release of growth-promoting molecules, such as fibroblast growth factor (FGF) to enhance angiogensis and wound healing (and may also be useful in Alzheimers disease and other dementia); blocking the activity of heparinase, an enzyme which participates in inflammatory processes and metases formation; modulation of bone metabolism, etc.

0/0

L28 ANSWER 8 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-046400 [07] WPIDS
DNC C1990-020190
TI Pharmaceutical compsn. contg. poly aromatic cpd. - for effecting **tissue** redistribution of bioactive peptide(s) and proteins normally bound to glycos amino glycan(s).
DC A96 B04
IN BENSASSON, S; EILAT, D
PA (HADA-N) HADASSAH MEDICAL ORGANIZATION
CYC 14
PI EP 354714 A 19900214 (199007)* EN 11p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
JP 02073019 A 19900313 (199016)
JP 02256610 A 19901017 (199048)
ADT EP 354714 A EP 1989-307825 19890801; JP 02073019 A JP 1989-209522 19890811; JP 02256610 A JP 1989-209998 19890814
PRAI IL 1988-87444 19880812; IL 1989-90993 19890716
AB EP 354714 A UPAB: 19930928
A pharmaceutical compsn. comprises a polymeric cpd. in which each monomeric unit contains about 3-10 aromatic rings and which has a M.W. of 1,000-20,000 Daltons, and a carrier.

In pref. polymers each monomeric unit contains 3-10 aromatic rings, more pref. 3-6, and these rings have one or more substituents on at least two of them. Substituents include -NRR1, -N=R, -OR, =O, -NO2, -COOR, halogen, -SO2OR, -SO2NHR, -OSO2OR and R where R is H or lower alkyl and R1 is H, lower alkyl or substd. phenyl. The polymeric cpds. include the salts and esters of the cpds.. The pref. M.W. is 2,000-4,000 Daltons, determined by gel permeation chromatography. Polymers ny known synthetic yes can be used and specified dyes include pt. halogenated and/or sulphonated, anazolene sodium, **eosine/bluish**, eosine yellowish, **erythrosine**, Evan's blue, fast green FCF, fuschine acid, iodophthalein sodium, methyl blue, **rose bengal**, sulphobromo-phthalein sodium, suramin sodium, krypton blue, krypton red, rosaniline chloride, crystal violet, methyl green, coomassie blue, basic fuschin, malachite green, brilliant green, aniline blue, brilliant cresyl blue, saframin O, ethyl violet, pararosaniline acetate and methyl violet. Pref. cpds. have the structure (I), and most pref. the structure (II), or are a salt or ester of the cpd., a, b and c are each independently zero or 1; dashed lines represent single or double bonds; each aromatic ring is

substd. by at least one of X, Y and Z which are selected from the substituents defined above; polymerisation is through carbon linkages.

USE - The compsn. is for affecting **tissue** redistribution of bioactive peptides and proteins normally bound to glycosamino glycans and for mimicking the action of glycosaminoglycans in various biological interactions. It can also be used as an anticoagulant. The compsn. is suitable for oral administration, the active ingredient being absorbed in the gastro intestinal tract.

0/0

L28 ANSWER 9 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1989-210013 [29] WPIDS
DNC C1989-093114
TI Physiological action enhancer to cure tumours with ultrasonic wave - comprises any cpd. which generates at least one type of active oxygen on ultrasonic irradiation.
DC B05
PA (UMEM-I) UMEMURA K
CYC 3
PI JP 01146829 A 19890608 (198929)* 4p
US 4971991 A 19901120 (199049)
JP 06029196 B2 19940420 (199414)
ADT JP 01146829 A JP 1987-305317 19871201; US 4971991 A US 1988-274109 19881121; JP 06029196 B2 JP 1987-305317 19871201
FDT JP 06029196 B2 Based on JP 01146829
PRAI JP 1987-305317 19871201
AB JP 01146829 A UPAB: 19930923
A physiological action enhancer for curing tumours by ultrasonic waves contains cpds. which generate one or more than one kind of active oxygen by irradiation with ultrasonic waves.

The cpd. used may be any cpd. which generates one or more than one kind of active oxygen by chemical reaction accompanied with irradiation of ultrasonic waves, pref. porphyrins e.g. hematoporphyrin, chlorine, water-soluble chlorophyll derivs., acridine derivs. e.g. methylene blude, fluorescein, acridine orange and neutral red, rhodamines e.g. **rose bengal** and tetracyclines. The cpds. may be made into the prepn.. by conventional means. The physiological action enhancer is used in the form of ointments, liniments, emulsions, injections, tablets, etc. The enhancer is administered orally or parenterally, and ultrasonic waves are then irradiated to the affected part. The dose is 1-50 mg/kg when administered by intravenous injection and 2-100 mg/kg when administerd orally.

USE/ADVANTAGE - Useful as a physiological action enhancer against tumour. By irradiation of ultrasonic waves, active oxygen as a superoxide radical and singlet oxygen are generated. No side effects are found. Useful for deep tumours.

0/0

L28 ANSWER 10 OF 10 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1988-140356 [20] WPIDS
DNN N1988-107142 DNC C1988-062584
TI Stabilised Romanowsky-type stain compsn. - with lysine or glycine as stabiliser.
DC B04 D16 E24 S03
IN KOETTERS, D; MALLIK, A; PLUTO, L
PA (FISH-N) FISHER SCI CO

CYC 1
PI US 4741898 A 19880503 (198820)* 3p
ADT US 4741898 A US 1985-718308 19850401
PRAI US 1985-718308 19850401
AB US 4741898 A UPAB: 19930923
Stabilised Romanowsky-type stain compsn. comprises (a) cationic dye component, namely Methylene Blue, Azure A, Azure B, Azure C or thionin; (b) anionic dye component namely Eosin Y, **Eosin B**, fluorescein, substd. fluorescein or Orange G; (c) 1-6C alcohol solvent; and (d) stabiliser (I) namely lysine, glycine or their acid addn. salts.

USE/ADVANTAGE - The compsn. is useful for staining biological **tissue** such as blood smears, malarial parasites and bone marrow. Use of (I) stabilises the stain compsn. against ppte. formation during storage, and esp. against progressive ppte. formation over weeks.
0/0

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      (FILE 'USPAT' ENTERED AT 14:48:14 ON 28 AUG 1999)
L1          1530 S (RADIOSENSITIZ? OR PHOTOSENSITIVE? OR PHOTOTHERAP?) (3A)
 AG
L2         81684 S (X(W)RAY? OR ION? RADIAT? OR RADIAT? THERAP? OR ELECTROM
AGN
L3             5 S HALOGEN? XANTHENE?
L4            11 S XANTHENE? (3A) (HALOGEN? OR IODIN? OR BROMIN?)
L5          1600 S ROSE BENGAL
L6             0 S 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
L7             0 S 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
L8             6 S ?TETRACHLORO (16W) TETRAIODOFLUORESCEIN?
L9             6 S ?TETRACHLORO (20W) TETRAIODOFLUORESCEIN?
L10        42246 S CANCER? OR TUMOR? OR DISEASE? TISSUE?
L11         2140 S ENCAPSULATE? (P) (MICELLE? OR NANOPARTICLE? OR LIPOSOME?
)
L12        51854 S ADMINIST? (P) (LOCAL? DELIVER? OR INJECT? OR FLOOD? OR S
PRA
L13          598 S AXIAL TOMOGRAPH?
L14        34830 S (HYDROPHIL? OR HYDROPHOB?) AND (RNA OR DNA OR AMINO ACID
? O
L15          346 S L1 AND L2
L16            0 S L15 AND L3
L17            0 S L15 AND L4
L18           11 S L15 AND L5
L19            0 S L1 AND L3
L20            0 S L1 AND L4
L21            0 S L1 AND L3
L22            0 S LL2 AND L3
L23            1 S L2 AND L4
L24            3 S L18 AND L10
L25            0 S L24 AND L11
L26            1 S L23 AND 12
L27            0 S L3 AND L10
L28            0 S L4 AND L10
L29          150 S L5 AND L10
L30            3 S L29 AND L15
L31            0 S L13 AND L5
L32          220 S L13 AND L10
L33            0 S L21 AND L5
L34            0 S L8 AND L10
L35            0 S L8 AND (L1 OR L2 OR L13)
L36           96 S L15 AND TISSUE?
L37           61 S L36 AND L12
L38            9 S L37 AND L11
L39            0 S L36 AND L3
L40            0 S L36 AND L4
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check 5,832,931 w/ Cancer Rose Bengal

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=> s (radiosensitiz? or photosensitive? or phototherap?) (3a) agent?

          255 RADIOSENSITIZ?
        50770 PHOTOSENSITIVE?
          344 PHOTOTHERAP?
       440915 AGENT?
L1        1530 (RADIOSENSITIZ? OR PHOTOSENSITIVE? OR PHOTOTHERAP?) (3A) AG
ENT
               ?

=> s (x(w)ray? or ion? radiat? or radiat? therap? or electromagnet? therap?
or photodynamic therap?)

       543083 X
       193790 RAY?
        75678 X(W)RAY?
       288676 ION?
       231939 RADIAT?
         7005 ION? RADIAT?
                (ION?(W)RADIAT?)
       231939 RADIAT?
        92047 THERAP?
         2196 RADIAT? THERAP?
                (RADIAT?(W)THERAP?)
       135207 ELECTROMAGNET?
        92047 THERAP?
           28 ELECTROMAGNET? THERAP?
                (ELECTROMAGNET?(W)THERAP?)
          684 PHOTODYNAMIC
        92047 THERAP?
          513 PHOTODYNAMIC THERAP?
                (PHOTODYNAMIC(W)THERAP?)
L2       81684 (X(W)RAY? OR ION? RADIAT? OR RADIAT? THERAP? OR ELECTROMAGN
ET?
                THERAP? OR PHOTODYNAMIC THERAP?)

=> s halogen? xanthene?

       172979 HALOGEN?
         3892 XANTHENE?
L3          5 HALOGEN? XANTHENE?
                (HALOGEN?(W)XANTHENE?)

=> s xanthene (3a) (halogen? or iodin? or bromin?)
<------User Break------>
u
SEARCH ENDED BY USER

=> s xanthene? (3a) (halogen? or iodin? or bromin?)

         3892 XANTHENE?
       172979 HALOGEN?
        61532 IODIN?
        79741 BROMIN?
L4         11 XANTHENE? (3A) (HALOGEN? OR IODIN? OR BROMIN?)

=> s rose bengal
```

```
          26163 ROSE
           1687 BENGAL
L5         1600 ROSE BENGAL
                  (ROSE(W)BENGAL)

=> s 4,5,6,7 tetrachloro 2',4',5',7' tetraiodofluorescein?

           2745 4,5,6,7
           4805 TETRACHLORO
            616 2',4',5',7'
             51 TETRAIODOFLUORESCEIN?
L6            0 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
                  (4,5,6,7(W)TETRACHLORO(W)2',4',5',7'(W)TETRAIODOFLUORESCE
IN?
                  )

=> s 4,5,6,7 tetrachloro 2',4',5',7' tetraiodofluorescein?

           2745 4,5,6,7
           4805 TETRACHLORO
            616 2',4',5',7'
             51 TETRAIODOFLUORESCEIN?
L7            0 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
                  (4,5,6,7(W)TETRACHLORO(W)2',4',5',7'(W)TETRAIODOFLUORESCE
IN?
                  )

=> s 4,5,6,7 tetrachloro 2#,4#,5#,7# tetraiodofluorescein?

           2745 4,5,6,7
           4805 TETRACHLORO

<------User Break------>
u
SEARCH ENDED BY USER

=> s ?tetrachloro (16w) tetraiodofluorescein?

           4828 ?TETRACHLORO
             51 TETRAIODOFLUORESCEIN?
L8            6 ?TETRACHLORO (16W) TETRAIODOFLUORESCEIN?

=> s ?tetrachloro (20w) tetraiodofluorescein?

           4828 ?TETRACHLORO
             51 TETRAIODOFLUORESCEIN?
L9            6 ?TETRACHLORO (20W) TETRAIODOFLUORESCEIN?

=> s cancer? or tumor? or disease? tissue?

          30170 CANCER?
          27801 TUMOR?
          92762 DISEASE?
         112635 TISSUE?
           1386 DISEASE? TISSUE?
                  (DISEASE?(W)TISSUE?)
L10       42246 CANCER? OR TUMOR? OR DISEASE? TISSUE?

=> s encapsulate? (p) (micelle? or nanoparticle? or liposome?)

          47976 ENCAPSULATE?
           5069 MICELLE?
            613 NANOPARTICLE?
           9559 LIPOSOME?
L11        2140 ENCAPSULATE? (P) (MICELLE? OR NANOPARTICLE? OR LIPOSOME?)
```

```
=> s adminster? (p) (local? deliver? or inject? or flood? or spray?)

<------User Break------>
u
SEARCH ENDED BY USER

=> s administ? (p) (local? deliver? or inject? or flood? or spray?)

        121059 ADMINIST?
        240487 LOCAL?
        335446 DELIVER?
           675 LOCAL? DELIVER?
                 (LOCAL?(W)DELIVER?)
        328618 INJECT?
         27726 FLOOD?
        211539 SPRAY?
L12      51854 ADMINIST? (P) (LOCAL? DELIVER? OR INJECT? OR FLOOD? OR SPRA
Y?)

=> s axial tomograph?

        354129 AXIAL
          7337 TOMOGRAPH?
L13        598 AXIAL TOMOGRAPH?
                 (AXIAL(W)TOMOGRAPH?)

=> s (hydrophil? or hydrophob?) and (rna or dna or amino acid? or protein? or
antibod? or ligand? or hapten? or receptor? or lipid?)

         61640 HYDROPHIL?
         58581 HYDROPHOB?
         19485 RNA
         32687 DNA
        169231 AMINO
        485369 ACID?
         58576 AMINO ACID?
                 (AMINO(W)ACID?)
         90415 PROTEIN?
         36371 ANTIBOD?
         28249 LIGAND?
          4958 HAPTEN?
         39672 RECEPTOR?
         24454 LIPID?
L14      34830 (HYDROPHIL? OR HYDROPHOB?) AND (RNA OR DNA OR AMINO ACID? O
R P
               ROTEIN? OR ANTIBOD? OR LIGAND? OR HAPTEN? OR RECEPTOR? OR L
IPI
               D?)
```

```
     (FILE 'USPAT' ENTERED AT 14:48:14 ON 28 AUG 1999)
L1          1530 S (RADIOSENSITIZ? OR PHOTOSENSITIVE? OR PHOTOTHERAP?) (3A)
 AG
L2         81684 S (X(W)RAY? OR ION? RADIAT? OR RADIAT? THERAP? OR ELECTROM
AGN
L3             5 S HALOGEN? XANTHENE?
L4            11 S XANTHENE? (3A) (HALOGEN? OR IODIN? OR BROMIN?)
L5          1600 S ROSE BENGAL
L6             0 S 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
L7             0 S 4,5,6,7 TETRACHLORO 2',4',5',7' TETRAIODOFLUORESCEIN?
L8             6 S ?TETRACHLORO (16W) TETRAIODOFLUORESCEIN?
L9             6 S ?TETRACHLORO (20W) TETRAIODOFLUORESCEIN?
L10        42246 S CANCER? OR TUMOR? OR DISEASE? TISSUE?
L11         2140 S ENCAPSULATE? (P) (MICELLE? OR NANOPARTICLE? OR LIPOSOME?
)
L12        51854 S ADMINIST? (P) (LOCAL? DELIVER? OR INJECT? OR FLOOD? OR S
PRA
L13          598 S AXIAL TOMOGRAPH?
L14        34830 S (HYDROPHIL? OR HYDROPHOB?) AND (RNA OR DNA OR AMINO ACID
? O
```

US PAT NO: 5,871,928 [IMAGE AVAILABLE] L24: 2 of 3
DATE ISSUED: Feb. 16, 1999
TITLE: Methods for nucleic acid analysis
INVENTOR: Stephen P. A. Fodor, 3863 Nathan Way, Palo Alto, CA 94303
Dennis W. Solas, 50 Gardenside Dr., #13, San Francisco, CA 94131
William J. Dower, 761 Partridge Ave., Menlo Park, CA 94025
APPL-NO: 08/873,034
DATE FILED: Jun. 11, 1997
ART-UNIT: 164
PRIM-EXMR: Stephanie W. Zitomer
LEGAL-REP: Pillsbury Madison & Sutro LLP

US PAT NO: 5,871,928 [IMAGE AVAILABLE] L24: 2 of 3

ABSTRACT:
The present invention provides methods and apparatus for sequencing, fingerprinting and mapping biological macromolecules, typically biological polymers. The methods make use of a plurality of sequence specific recognition reagents which can also be used for classification o

US PAT NO: 5,871,928 [IMAGE AVAILABLE] L24: 2 of 3

DETDESC:

DETD(82)

In . . . the protection are described below and in related Pirrung et al. (1992) U.S. Pat. No. 5,143,854. In a preferred embodiment, **photosensitive** protecting **agents** will be used and the regions of activation or deactivation may be controlled by electro-optical and optical methods, similar to. . .

DETDESC:

DETD(86)

The . . . benzyloxy carbonyl, 5-bromo-7-nitroindolinyl, O-hydroxy-.alpha.-methyl cinnamoyl, and 2-oxymethylene anthraquinone. Examples of activators include ion beams, electric fields, magnetic fields, electron beams, **x-ray**, and other forms of electromagnetic radiation.

DETDESC:

DETD(239)

The . . . tool to test the combination of presence, of a plurality of different assays from a biological sample. For example, a **cancerous** condition may be indicated by a combination of various different properties found in the blood. For example, a **cancerous** condition may be indicated by a combination of expression of various soluble antigens found in the blood along with a. . .

DETDESC:

DETD(279)

In . . . of the cells for which this would be most useful will be immobile cells found in particular tissues or organs. **Tumor** cells will be diagnosed or detected using these fingerprinting techniques. Coupled with a temporal change in structure, developmental classes may. . .

DETDESC:

DETD(281)

In . . . population allows detailed statistical analysis to be made, thereby correlating particular medical conditions with particular markers, typically antigenic or genetic. **Tumor** specific antigens will be identified using the present invention.

DETDESC:

DETD(362)

A . . . p-bis[2-(4-methyl-5-phenyl-oxazolyl)]benzene; 6-dimethylamino-1,2-benzophenazin; retinol; bis(3'-aminopyridinium)

1,10-decandiyl diiodide; sulfonaphthylhydrazone of hellibrienin; chlorotetracycline; N-(7-dimethylamino-4-methyl-2-oxo-3-chromenyl)maleimide; N-[p-(2-benzimidazolyl)-phenyl]maleimide; N-(4-fluoranthyl)maleimide; bis(homovanillic acid); resazarin; 4-chloro-7-nitro-2,1,3-benzooxadiazole; merocyanine 540; resorufin; **rose bengal**; and 2,4-diphenyl-3(2H)-furanone.

DETDESC:

DETD(416)

In . . . distinguishing different species of animals or plants. In fact, microbial identification may become dependent on characterization of the genetic content. **Tumors** or other cells exhibiting abnormal physiology will be detectable by use of the present invention. Also, knowing the genetic fingerprint. . .

DETDESC:

DETD(645)

The . . . For example, in some embodiments it may be desirable to use protective groups which are sensitive to electron beam irradiation, **x-ray** irradiation, in combination with electron beam lithograph, or **x-ray** lithography techniques. Alternatively, the group could be removed by exposure to an electric current. The scope of the invention should,. . .

US PAT NO: 5,879,656 [IMAGE AVAILABLE] L38: 2 of 9

SUMMARY:

BSUM(7)

Although . . . cells. Theoretically, targeting permits uptake by cells of cytotoxic agents at concentrations which do not produce serious toxicities in normal **tissues**. Also, selective binding to targeted tumor cells facilitates detection of occult tumor and is therefore useful in designing imaging agents.. . .

SUMMARY:

BSUM(10)

Due . . . cells but the antigens are nonetheless often present in normal cells. Thus, antibodies to such determinants can react with non-neoplastic **tissues**, resulting in significant toxicities. Also, antibodies are relatively large molecules and consequently, often evoke an immune response in patients. These. . .

DETDESC:

DETD(12)

As used herein, the term "therapeutic agent" is meant to refer to chemotherapeutics, toxins, radiotherapeutics, targeting **agents** or **radiosensitizing agents**.

DETDESC:

DETD(17)

As used herein, the term **"radiosensitizing agent"** is meant to refer to agents which increase the susceptibility of cells to the damaging effects of **ionizing radiation**. A **radiosensitizing agent** permits lower doses of radiation to be administered and still provide a therapeutically effective dose.

DETDESC:

DETD(33)

Therapeutic . . . targeted to metastatic disease. These conjugated compounds include ST receptor binding moieties which do not bind to cells of normal **tissue** in the body except cells of the intestinal tract since the cells of other **tissues** do not possess ST receptors. Unlike normal colorectal cells and localized colorectal cancer cells, metastasized colorectal cancer cells are accessible. . . to substances administered outside the intestinal tract, for example administered in the circulatory system. The only ST receptors in normal **tissue** exist in the apical membranes of intestinal mucosa cells and these receptors are effectively isolated from the targeted cancer chemotherapeutics. . .

DETDESC:

DETD(83)

Radiosensitizing agents are substances that increase the sensitivity of cells to radiation. Examples of **radiosensitizing agents** include nitroimidazoles, metronidazole and misonidazole (see: DeVita, V. T. Jr. in Harrison's Principles of Internal Medicine, p.68, McGraw-Hill Book Co., N.Y. 1983, which is incorporated herein by reference). The conjugated compound that comprises a **radiosensitizing agent** as the active moiety is administered and localizes at the metastasized cell. Upon exposure of the individual to radiation, the **radiosensitizing agent** is "excited" and causes the death of the cell.

DETDESC:

DETD(85)

Examples of radionuclides useful as toxins in **radiation therapy** include: .sup.47 Sc, .sup.67 Cu, .sup.90 Y, .sup.109 Pd, .sup.123 I, .sup.125 I, .sup.131 I, .sup.186 Re, .sup.188 Re, .sup.199. . .

DETDESC:

DETD(95)

The . . . stability (e.g., buffers and preservatives). The formulation is sterilized by commonly used techniques. For example, a parenteral composition suitable for **administration** by **injection** is prepared by dissolving 1.5% by weight of active ingredient in 0.9% sodium chloride solution.

DETDESC:

DETD(113)

Another . . . of the invention relates to unconjugated compositions which comprise an ST receptor binding ligand and an active agent. For example, **liposomes** are small vesicles composed of lipids. Drugs can be introduced into the center of these vesicles. The outer shell of these vesicles comprise an ST receptor binding ligand. **Liposomes** Volumes 1, 2 and 3 CRC Press Inc. Boca Raton Fla., which is incorporated herein by reference, disclose preparation of **liposome-encapsulated** active agents which include targeting agents that correspond to ST receptor ligand in the outer shell. Unconjugated compositions which comprise an ST receptor ligand in the matrix of a **liposome** with an active agent inside include such compostions in which the ST receptor ligand is selected from the group consisting. . .

DETDESC:

DETD(117)

Liposomes are small vesicles composed of lipids. Genetic constructs which encode proteins that are desired to be expressed in ST receptor-bearing. . . these vesicles. The outer shell of these vesicles comprise an ST receptor ligand, in some embodiments preferably an ST peptide. **Liposomes** Volumes 1, 2 and 3 CRC Press Inc. Boca Raton Fla., which is incorporated herein by reference, disclose preparation of **liposome-encapsulated** active agents which include antibodies in the outer shell. In the present invention, an ST receptor ligand such as for. . . to the antibodies in the outer shell. Unconjugated compositions which comprise an ST receptor ligand in the matrix of a **liposome** with an active agent inside include such compositions in which the ST receptor ligand is selected from the group consisting. . .

CLAIMS:

CLMS(9)

9. The method of claim 1 wherein said an active moiety is selected from the group consisting of chemotherapeutics, toxins and **radiosensitizing agents**.

CLAIMS:

CLMS(12)

12. The method of claim 11 wherein said active moiety is selected from the group consisting of chemotherapeutics, toxins and **radiosensitizing agents**.

US PAT NO: 5,840,276 [IMAGE AVAILABLE] L38: 3 of 9

ABSTRACT:
Dispersions . . . phase suitable for infusion into a human or other animal, the drops being vaporizable in a selected body location by **ionizing radiation** or ultrasound. The dispersions can be used to form diagnostic contrast agents, to improve diffusion of drugs, to occlude capillaries. . .

SUMMARY:

BSUM(4)

Selective . . . of cancer deaths in the United States today. Almost without exception, anticancer drugs are toxic to cells of critical normal **tissues**, as well as to cancer cells. The intensity of treatment with these drugs is limited by the ability of normal **tissues** (and the patient) to tolerate the therapy, rather than by the amount of drug needed for optimal treatment of the. . .

SUMMARY:

BSUM(5)

Selective . . . tried in laboratory and clinical studies to improve the treatment of solid cancers. Direct topical application of drugs and intratumoral **injection** of drugs has had limited success, largely because the diffusion of drug from the **administration** site is inadequate. Selective infusion of tumors through a major artery supplying the tumor has been effective only in some. . .

SUMMARY:

BSUM(6)

Different approaches have been tried for the purpose of "targeting" intravenously **injected** drugs. Ibid. Drugs have been attached to antibodies directed against specific tumor antigens. Drugs have been **encapsulated** in **liposomes**, starch microspheres, or other encapsulation vehicles in the hopes that this would protect the drug from inactivation in the blood. . . and that these particles would lodge selectively in the abnormally tortuous tumor blood vessels. Attempts have been made to target **liposomes**, for example by developing magnetic **liposomes** and applying magnets to the surface of the tumor or by **administering** heat-sensitive **liposomes** and delivering heat in order to cause a tumor to become hyperthermic. Limited success has been observed. Drug release in non-target **tissues** remains a limitation.

SUMMARY:

BSUM(10)

Another . . . administering the dispersions intravenously and subjecting the selected target location with a localized or localizable source of radiation, most preferably **x-ray** or gamma ray, or ultrasound capable of nucleating the superheated drops to transform them into the vapor phase. The transformation. . .

SUMMARY:

BSUM(12)

This invention includes dispersions comprising drops of a superheated liquid dispersed in an **injectable** host fluid such as intravenous fluid. The dispersions are infusable, that is, suitable for infusion into the body of a. . . have sufficient immiscibility with body fluid of patients, whether human or other animals, to retain their integrity as drops after **administration** to permit localized vaporization and sufficient immiscibility with any intravenous or other host fluid used for infusion of the drops to retain their integrity as drops during preparation, storage, if any, and **administration**. Generally, solubility in aqueous host and body fluids should not exceed a few percent during the pertinent time period.

SUMMARY:

BSUM(14)

The . . . this purpose. Most preferably the degree of superheat is very high for nucleation by common medical radiation sources such as **x-rays** or gamma rays, in the range of about 60-80 Celsius degrees, near but at least a few degrees below the. . . of -15.degree. C. to -30.degree. C. at atmospheric pressure will be found to be suitable for nucleation in humans by **x-rays**. By "radiation" I mean **ionizing radiation** (such as **x-rays**, alpha, beta, gamma and neutron), particles or waves capable of causing an electron to be removed from an atom or. . .

SUMMARY:

BSUM(15)

The . . . oxygen. Drops may vaporize in a selected location to form bubbles that serve as contrast agents for diagnostic imaging, including **x-ray**, ultrasound and MRI. Some capillary regions may be entered by drops where larger bubbles, if preformed, would not enter. Bubbles. . .

SUMMARY:

BSUM(18)

As the superheated drops are subjected to **ionizing radiation** or ultrasound, they vaporize (boil), thereby forming bubbles and releasing any drug with which they are doped into the local. . .

SUMMARY:

BSUM(21)

The . . . the temperature of use), then the drops of the tested composition will be triggered at body temperature by a simple **x-ray** or gamma ray source, commonly available in hospitals. For

less superheat, a neutron source or perhaps even a proton source is needed to trigger the drops at body temperature. The use of **x-rays** has obvious advantages for practical applications. Therefore, the composition selected for testing was made to be sensitive to **x-rays** and gamma rays at body temperature (37.degree. C.).

SUMMARY:

BSUM(33)
A) An **x-ray** machine, such as used in diagnostic **x-rays**, is a directable, and hence, localizable source of radiation external to the body;

SUMMARY:

BSUM(34)
B) Radiological sources, for example, cobalt 60, producing gamma **x-rays**, are also directable sources of external radiation;

SUMMARY:

BSUM(36)
D) A medical accelerator source of radiation (either **x-rays** or high energy electrons) is also a directable source of external radiation that will penetrate into **tissue** to trigger drops into bubbles; and

SUMMARY:

BSUM(39)

Ionizing radiation is useful to trigger the drops. The use of **ionizing radiation** as the triggering agent has several advantages. First, there is growing evidence than regimens combining concomitant radiation and drugs are. . . more effective that regimens using sequential treatments. Preferred drugs for combined treatment with radiation are radiation sensitizers or bioreductive alkylating **agents. Radiosensitizers** such as misonidazole or etanidazole have proven effective in increasing the radiocurability of tumors in experimental animals. They have shown. . . of drug treatments have been severely limited by toxicities which reflect the cumulative dose of drug delivered to certain normal **tissues** distant from the radiation field. The drug delivery system of this invention minimizes drug delivery to normal **tissues** with such treatment.

SUMMARY:

BSUM(40)

Bioreductive . . . largely by the toxicity of the drug to marrow and by the possibility of toxicity to lung, kidney, and other **tissues** outside the radiation field. Better targeting of drug delivery by the system and method of this invention affords a way. . .

SUMMARY:

BSUM(41)

Delivery of drugs to a tumor by vaporizing superheated carrier drops using **ionizing radiation** also offers many technical advantages. Modern radiotherapy treatment planning techniques allow the delivery of radiation to the tumor volume with. . .

SUMMARY:

BSUM(43)

Modern . . . mechanical agitation of bubbles enhances diffusion, an advantage in distributing a delivered drug whether to nearby tumor or other targeted **tissue**. Moreover, the fact that drug-doped drops and triggered bubbles can be imaged by ultrasound is of value in non-invasively documenting drug distribution and in delineating **tissue** (e.g. tumor) structure.

SUMMARY:

BSUM(47)
c) . . . contrast agents, because bubbles in vessels and capillaries are good contrast agents and, therefore, can be effectively imaged (e.g. with **x-ray**, ultrasound, or MRI);

SUMMARY:

BSUM(50)
f) . . . and duty cycles and in an appropriate frequency range (e.g. from 20 kHz to 10 MHz) increasing drug diffusion into **tissue** by virtue of mechanical action of the sound field on the bubbles, thereby making drug treatment more efficacious.

DETDESC:

DETD(24)

The . . . radiation was given to trigger bubble formation, c) cultures treated with both the drop composition and radiation (1 Gy of **x-rays** from a 250 kV **x-ray** source, delivered 5 min after the addition of the drops to trigger boiling), and d) cultures receiving radiation alone. For. . . the amounts of dispersion tested (20-50 .mu.l), neither the intact drops nor the drops without drug triggered to lysis by **x-rays** altered in a significant way either the number of intact cells in the cultures or the viability of the cells,. . .

DETDESC:

DETD(29)

The . . . drops can be doped with drugs and encapsulated in an aqueous diluent, and that these drops can be triggered by **x-ray** irradiation at levels significantly lower than therapeutic regimens of radiation (and also by diagnostic levels of ultrasound), thereby releasing their. . .

DETDESC:

DETD(31)

Our work indicates the drop material can be triggered in great enough proportions with amounts of **x-rays** significantly lower than therapeutic doses. We found that 1 .mu.g of drug carried in approximately 10 mg of drop material. . . could be infused in 2.5 minutes at a rate of 0.1 ml per minute. If exposed to 1 Gy of **x-rays** at the position of a tumor, over 2 million bubbles, or approximately one half of the drops, would be triggered,. . . release adequate amounts of chemotherapeutic drug into a tumor, releasing significantly less drug outside the tumor region, thereby sparing normal **tissue** and allowing for a spatial partitioning.

CLAIMS:

CLMS(1)

I . . .

at least 17 Celsius degrees, said amount of superheat being sufficient to permit their in-body nucleation by a level of **ionizing radiation** or ultrasound tolerable to said body.

CLAIMS:

CLMS(14)

14. . . .
infusing a dispersion according to claim 5; and
b) selectively subjecting said body location to energy from the group consisting of **ionizing radiation** and ultrasound to vaporize the drops of said dispersion, thereby releasing said drug at said body location.

CLAIMS:

CLMS(15)

15. The method according to claim 14, wherein said energy is **ionizing radiation**.

CLAIMS:

CLMS(20)

20. The method according to claim 19 wherein said energy is **ionizing radiation**.

CLAIMS:

CLMS(26)

26. . . . selected body location, the improvement comprising injecting intravenously a dispersion according to claim 1 and subjecting said body location to **ionizing radiation** or ultrasound to vaporize the drops of said dispersion, thereby producing at said location bubbles which serve as contrast agents.

CLAIMS:

CLMS(28)

28. . . . a dispersion according to claim 1 and selectively subjecting said body location to energy selected from the group consisting of **ionizing radiation** and ultrasound to vaporize the drops of said dispersion.

US PAT NO: 5,827,880 [IMAGE AVAILABLE] L38: 5 of 9

ABSTRACT:
The . . . of salen-metal complexes in a form suitable for pharmaceutical administration to treat or prevent a disease associated with cell or **tissue** damage produced by free radicals such as superoxide, and cosmetic and free radical quenching formulations of salen metal compounds.

SUMMARY:

BSUM(2)

The . . . antioxidants as preservatives and oxyradical quenching

agents in hydrocarbons, methods for using the small molecule antioxidants for targeted protection of **tissues** and/or cell types during cancer chemotherapy, and methods for using the small molecule antioxidants to prevent toxicologic damage to individuals. . . are also used for preventing oxidative damage in human transplant organs and for inhibiting reoxygenation injury following reperfusion of ischemic **tissues**. The compositions and methods of the invention are also useful for chemoprevention of chemical carcinogenesis and alteration of drug metabolism. . .

SUMMARY:

BSUM(6)

Biological . . . acid, and metal-binding proteins. Various antioxidants, being both lipid and water soluble, are found in all parts of cells and **tissues**, although each specific antioxidant often shows a characteristic distribution pattern. The so-called ovothiols, which are mercaptohistidine derivatives, also decompose peroxides. . .

SUMMARY:

BSUM(7)

Free . . . and other disease. Oxyradical can react with proteins, nucleic acids, lipids, and other biological macromolecules producing damage to cells and **tissues**, particularly in the critically ill patient.

SUMMARY:

BSUM(9)

Free . . . respiration, cytochrome P-450-catalyzed monooxygenation reactions of drugs and xenobiotics (e.g., trichloromethyl radicals, CCl.sub.3., formed from oxidation of carbon tetrachloride), and **ionizing radiation**. For example, when **tissues** are exposed to gamma radiation, most of the energy deposited in the cells is absorbed by water and results in. . . radical, which is believed to be an essential factor in producing the cytotoxic effect of activated neutrophils. Reperfusion of ischemic **tissues** also produces large concentrations of Oxyradical, typically superoxide (Gutteridge J. M. C. and Halliwell B. (1990) Arch. Biochem. Biophys. 283:. . .

SUMMARY:

BSUM(10)

Oxygen, . . . the neutrophil "respiratory burst", superoxide anion is generated by the membrane-bound NADPH oxidase. ROS are also believed to accumulate when **tissues** are subjected to ischemia followed by reperfusion.

SUMMARY:

BSUM(22)

In an effort to prevent the damaging effects of oxyradical formation during reoxygenation of ischemic **tissues**, a variety of antioxidants have been used.

SUMMARY:

BSUM(28)

Based . . . inexpensive to manufacture, stable, and possess advantageous pharmacokinetic properties, such as the ability to cross the blood-brain barrier and penetrate **tissues**. Such versatile antioxidants would find use as pharmaceuticals, chemoprotectants, and possibly as dietary supplements. It is one object of the. . .

SUMMARY:

BSUM(29)

It . . . isoprene rubbers, other rubber analogs, oils and waxes, cosmetic bases, animal fats, petroleum and petrochemicals and distillates, polymerizable resins, dyes, **photosensitive agents**, flavor **agents**, adhesives, sealants, polymer precursors, and the like. Also encompassed in the invention are salen-metal antioxidants and methods for inhibiting oxyradical-mediated. . .

SUMMARY:

BSUM(33)

The . . . are typically salen-manganese complexes, such as Mn(III)-salen complexes. The invention provides methods for preventing or reducing ischemic/reperfusion damage to critical **tissues** such as the myocardium and central nervous system. The invention also provides methods for preventing or reducing cellular damage resulting. . .

SUMMARY:

BSUM(34)

In . . . (2) for preserving organs for transplant in an anoxic, hypoxic, or hyperoxic state prior to transplant, (3) for protecting normal **tissues** from free radical-induced damage consequent to exposure to **ionizing radiation** and/or chemotherapy, as with bleomycin, (4) for protecting cells and **tissues** from free radical-induced injury consequent to exposure to xenobiotic compounds which form free radicals, either directly or as a consequence of monooxygenation through the cytochrome P-450 system, (5) for enhancing cryopreservation of cells, **tissues**, organs, and organisms by increasing viability of recovered specimens, and (6) for prophylactic administration to prevent: carcinogenesis, cellular senescence, cataract. . .

SUMMARY:

BSUM(36)

In . . . the invention at a concentration of at least 1 nM but not more than about 100 mM is formulated for **administration**, usually at a concentration of about 0.1 to 10 mM, typically by intravenous route, to a patient undergoing or expected. . . antineoplastic or antihelminthic chemotherapy employing a chemotherapeutic agent which generates free radicals, (3) endotoxic shock or sepsis, (4) exposure to **ionizing radiation**, (5) exposure to exogenous chemical compounds which are free radicals or produce free radicals, (6) thermal or chemical burns or. . . and myocardial irrigation. Nonaqueous formulations, such as lipid-based formulations are also provided, including stabilized emulsions. The antioxidant salen-metal compositions are **administered** by various routes, including intravenous **injection**, intramuscular **injection**, subdermal **injection**, intrapericardial **injection**, surgical irrigation, topical application, ophthalmologic application, lavage, gavage, enema, intraperitoneal infusion, mist inhalation, oral rinse, and other routes, depending upon. . .

SUMMARY:

BSUM(44)

The . . . may be effected by means other than those listed herein. Further, the peroxide-induced condition may involve cataracts, inflammation of a **tissue**, ischemia, an allergic reaction, or pathology caused by oxidative stress. Where the peroxide-induced condition involves cataracts, administration is effected by,. . .

DETDESC:

DETD(63)

The compositions for parenteral **administration** will commonly comprise a solution of an antioxidant salen-transition metal complex or a cocktail thereof dissolved in an acceptable carrier,. . . 100 mM and will be selected primarily based on fluid volumes, viscosities, etc., in accordance with the particular mode of **administration** selected. Most usually, the antioxidant salen-metal complex is present at a concentration of 0.1 mM to 10 mM. For example, a typical formulation for intravenous **injection** comprises a sterile solution of an antioxidant salen-metal complex (e.g., C7) at a concentration of 5 mM in Ringer's solution.. . . aqueous vehicle comprising a detergent or other lipophilic agent (e.g., Tween, NP-40, PEG); alternatively, the antioxidant salen complexes may be **administered** as a suspension in an aqueous carrier, or as an emulsion.

DETDESC:

DETD(64)

Thus, a typical pharmaceutical composition for intramuscular **injection** could be made up to contain 1 ml sterile buffered water, and about 1-100 mg of antioxidant salen-transition metal complex(es).. . . antioxidant salen-transition metal complex(es). Lipophilic agents may be included in formulations of lipophilic salen-metal complexes. Actual methods for preparing parenterally **administrable** compositions will be known or apparent to those skilled in the art and are described in more detail in, for. . .

DETDESC:

DETD(66)

The compositions containing the present antioxidant salen-transition metal complex(es) or cocktails thereof can be **administered** for prophylactic and/or therapeutic treatments. In therapeutic application, compositions are **administered** to a patient already affected by the particular free radical-associated disease, in an amount sufficient to cure or at least. . . this use will depend upon the severity of the condition, the general state of the patient, and the route of **administration**, but generally range from about 1 mg to about 10 g of antioxidant salen-transition metal complex(es) per dose, with dosages. . . treating acute myocardial ischemia/reoxygenation episodes, about 100 to 1000 mg of a antioxidant salen metal complex (e.g., C7) may be **administered** systemically by intravenous infusion; at least about 10 mg to 500 mg of antioxidant salen-metal complex(es) may be **administered** by intrapericardial **injection** to provide elevated local concentrations of SOD activity in the myocardium.

DETDESC:

DETD(71)

The dosage of SOD-mimetic salen-metal complex(es) will vary with each particular application. Typically, the composition is **administered** either systemically or topically. Systemic **administration** includes per os and parenteral routes; topical **administration** includes in situ applications. The in situ means includes, for example, **administering** an SOD-mimetic salen-metal complex by endoscopic bolus wash and/or paravenous **injection**, or in the case of lower GI treatments, by enema. Parenteral routes may include, for example, subcutaneous, intradermal, intramuscular, and. . . salen-metal complex(es) will range from about 2 to 5,000 mg or more, typically 10 to 1000 mg, depending on the **administration** interval and route, which can range from a single oral dose, parenteral dose and/or topical dose to multiple oral doses,. . .

DETDESC:

DETD(75)

According . . . the group consisting of: N-2-mercaptopropionylglycine, N-acetylcysteine, glutathione, dimethyl thiourea, desferrioxamine, mannitol, .alpha.-tocopherol, ascorbate, allopurinol, 21-aminosteroids, calpain inhibitors, glutamate receptor antagonists, **tissue** plasminogen activator, streptokinase, urokinase, nonsteroidal anti-inflammatory agent, cortisone, and carotenoids. Antioxidant salen-Mn complexes may also be administered in conjunction with. . .

DETDESC:

DETD(80)

The . . . include, for example, solid, semi-solid and liquid dosage forms, such as tablets, pills, powders, liquid solutions or suspensions, liposome preparations, **injectable** and infusible solutions. The preferred form depends on the intended mode of **administration** and therapeutic application. Typically, a sterile solution of a salen-metal complex in an aqueous solvent (e.g., saline) will be **administered** intravenously. The compositions also preferably include conventional pharmaceutically acceptable carriers and adjuvants which are known to those of skill in the art. See, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Co.: Easton, Pa., 17th Ed. (1985). Generally, **administration** will be by oral or parenteral (including subcutaneous, intramuscular, intravenous, and intradermal) routes, or by topical application or infusion into a body cavity, or as a bathing solution for **tissues** during surgery.

DETDESC:

DETD(89)

Parenteral **administration** is generally characterized by **injection**, either subcutaneously, intramuscularly or intravenously. **Injectables** can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to **injection**, or as emulsions. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol or the like. In addition, if desired, the pharmaceutical compositions to be **administered** may also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents and the. . .

DETDESC:

DETD(93)

Antioxidant salen-metal complex(es) can also be added to rinse or storage solutions for organs and **tissues**, such as for organ transplantation or for surgical rinses. For example, excised organs are often placed in a preservation solution. . .

DETDESC:

DETD(94)

Typically . . . salen-metal complex can be used to provide enhanced storage or irrigation of organs (e.g., kidney, liver, pancreas, lung, fetal neural **tissue**, heart, vascular grafts, bone, ligament, tendon, skin) which is believed to enhance the viability of the **tissue** and increase resistance to oxidative damage (e.g., as a consequence of ischemia/reperfusion).

DETDESC:

DETD(96)

Alternatively, . . . to catalyze the decomposition of reactive oxygen species can be used to advantage to inhibit or slow damage to biological **tissues** and cells. For example, benzoyl peroxide is a widely used treatment for acne lesions; excessive or inappropriate application of benzoyl. . . treated by local (or if desired, systemic) administration of an antioxidant salen-metal complex (e.g., C7). Similarly, oxyradical-induced damage to connective **tissues** (e.g., collagen) attendant to exposure to UV light, cigarette smoking, and senescence may be reduced by administration of an antioxidant. . .

DETDESC:

DETD(98)

Antioxidant salen-transition metal complexes, typically antioxidant salen-Mn complexes, such as compound C7, are used to protect cells and **tissues** from free radical-producing agents, such as **ionizing radiation** and chemotherapeutic agents (e.g., bleomycin). Preferably, a protective dosage comprising at least about 1 .mu.g of salen-Mn complex/kg bodyweight is **administered** by one or more of several routes (e.g., oral, intraveneous, intraperitoneal, intragastric lavage, enema, portal vein infusion, topical, or inhalation of mist), preferably by **injection** of liposomes or immunoliposomes for targeted delivery of the antioxidant salen-Mn complexes to protect normal cells, for example, against free. . . commencement, and preferably within about 3-6 hours of commencement of the chemotherapy and/ or radiotherapy. Antioxidant salen-Mn may be continually **administered** to the patient during the course of therapy.

DETDESC:

DETD(99)

For example, a solution of an antioxidant salen-metal complex can be **encapsulated** in **micelles** to form immunoliposomes (U.S. Pat. No. 5,043,164, U.S. Pat. No. 4,957,735, U.S. Pat. No. 4,925,661; Connor and Huang (1985) J.. . .

DETDESC:

DETD(106)

In . . . anti-inflammatory agent in a cosmetic base or dental linament (periodontal disease) for topical application for local prevention of inflammation and/or **tissue** damage consequent to

inflammation. A variety of steroidal and non-steroidal anti-inflammatory agents can be combined with an antioxidant salen-metal compound.

DETDESC:

DETD(159)

Rats received an intramuscular **injection** of 0.25 ml of an iron-dextran solution (100 g iron hydroxide, 99 g dextran, water up to 11) every third day during a 5-week period to achieve a significant iron overload in cardiac **tissue**. At the end of this treatment, rats were anesthetized with sodium pentobarbital (40 mg/kg) and heparin (1,000 IU/kg) was **administered** via a femoral vein. Hearts were then removed and rapidly perfused through the aorta according to the technique described by. . .

DETDESC:

DETD(191)

MPTP in mice. Adult male CFW mice (25-33 g) were **administered** two **injections** of MPTP dissolved in normal saline (40 mg/kg, s.c.) 24 hours apart. A group of animals also received C7 in three **injections** (33 mg/kg, s.c.) **administered** 24 hours apart, starting 1 day before the onset of MPTP treatment. Animals were sacrificed 7 days after the first MPTP **injection**, and neuronal pathology was assessed by the binding of .sup.3 H-mazindol, a ligand for the dopamine transporter, to 10 mm. . .

DETDESC:

DETD(205)

Synthetic catalytic scavengers of reactive oxygen species (ROS) may have clinical value in alleviating **tissue** damage associated with numerous acute and chronic diseases. Example 1 demonstrates that synthetic salen manganese complexes have superoxide dismutase (SOD) activity. One of these compounds, C7, has been found to be protective in several models for ROS-associated **tissue** injury. In this example, the catalytic properties of C7, in particular, are further characterized demonstrating that it also utilizes hydrogen. . .

DETDESC:

DETD(210)

0-Vanillin, . . . purchased from EM Sciences (Gibbstown, N.J.). The XTT reagent was obtained from Boehringer Mannheim, Inc. (Indianapolis, Ind.). All components of **tissue** culture media were purchased from BioWhittaker (Walkersville, Md.) and **tissue** culture plastic ware was from Corning (Corning, N.Y.). All other chemicals were obtained from Sigma Chemicals (St. Louis, Mo.).

DETDESC:

DETD(224)

Human dermal fibroblasts (HF cells) were obtained from the American type **tissue** Culture Collection at passage 1 and cultured and propagated in a medium (HF medium) consisting of Dulbecco's Modified Eagle's Medium. . . incubated with HF medium containing glucose oxidase (0.019 units/ml) along with test compounds, as indicated, for 18 hr in the **tissue** culture incubator. Fresh HF medium was then added and cell viability assessed using the XTT reagent as described above. For. . .

DETDESC:

DETD(243)

In **tissues**, ROS promote **tissue** destruction in part through oxidative damage to cellular macromolecules, in particular, by inducing lipid peroxidation. The salen manganese compounds were tested for the ability to protect brain **tissue** from lipid peroxidation induced by incubating brain homogenates with iron in an oxygen-rich atmosphere. Malonyldialdehyde, a byproduct of lipid peroxidation,. . .

DETDESC:

DETD(246)

Salen . . . cells due to its intracellular decomposition to alkoxyl and methoxyl free radicals. It has been reported that SOD, particularly when **encapsulated** into **liposomes**, protects hepatocytes from t-BHP toxicity, implying that intracellular superoxide may play a role in the cytotoxicity of this organic hydroperoxide.. . .

DETDESC:

DETD(253)

The . . . pathology. In Example 1, C7 has already been shown to be protective in much more complex biological models for ROS-induced **tissue** damage than those employed in Example 2.

US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9
DATE ISSUED: Jul. 14, 1998
TITLE: Compositions and methods useful for inhibiting cell death and for delivering an agent into a cell
INVENTOR: Ban An Khaw, Milton, MA
Vladmir P. Torchilin, Charlestown, MA
Jagat Narula, Brookline, MA
Imran Vural, Brookline, MA
ASSIGNEE: Northeastern University, Boston, MA (U.S. corp.)
APPL-NO: 08/427,676
DATE FILED: Apr. 24, 1995
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Weingarten, Schurgin, Gagnebin & Hayes LLP

US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9

ABSTRACT:
The invention relates to methods of salvaging a target cell from cell death, comprising contacting a target cell having a disrupted cell membrane with a specific affinity reagent-liposome conjugate in an amount effective and for a time sufficient to allow the conjugate to prevent cell death due to membrane disruption; and determining the viability of the target cell. Methods of delivering a selected agent into a damaged target cell for diagnosis and therapy are also disclosed.

US PAT NO: 5,696,109 [IMAGE AVAILABLE] L38: 7 of 9
DATE ISSUED: Dec. 9, 1997
TITLE: Synthetic catalytic free radical scavengers useful as antioxidants for prevention and therapy of disease
INVENTOR: Bernard Malfroy-Camine, Arlington, MA
Susan Robin Doctrow, Roslindale, MA
ASSIGNEE: Eukarion, Inc., Bedford, MA (U.S. corp.)
APPL-NO: 08/485,489
DATE FILED: Jun. 7, 1995
ART-UNIT: 125
PRIM-EXMR: William R. A. Jarvis
LEGAL-REP: Townsend and Townsend and Crew LLP

US PAT NO: 5,696,109 [IMAGE AVAILABLE] L38: 7 of 9

ABSTRACT:
The invention provides antioxidant salen-metal complexes, compositions of such antioxidant salen-metal complexes having superoxide activity, catalase activity, and/or peroxidase activity, compositions of salen-metal complexes in a form suitable for pharmaceutical administration to treat a disease associated with cell or **tissue** damage produced by free radicals such as superoxide, and cosmetic and free radical quenching formulations of salen metal compounds.

US PAT NO: 5,641,754 [IMAGE AVAILABLE] L38: 8 of 9
DATE ISSUED: Jun. 24, 1997
TITLE: Antisense oligonucleotide compositions for selectively killing cancer cells

INVENTOR: Patrick L. Iversen, Omaha, NE
ASSIGNEE: The Board of Regents of The University of Nebraska, Lincoln, NE (U.S. corp.)
APPL-NO: 08/179,655
DATE FILED: Jan. 10, 1994
ART-UNIT: 189
PRIM-EXMR: John LeGuyader
LEGAL-REP: Zarley, McKee, Thomte, Voorhees & Sease

US PAT NO: 5,641,754 [IMAGE AVAILABLE] L38: 8 of 9

ABSTRACT:
The present invention relates to methods and compositions for the treatment of cancer using an oligonucleotide and an hydroxyl radical up-regulator. The oligonucleotide is characterized by its ability to down-regulate the path by which the cell repairs oxidative damage to its DNA. Thus, the oligonucleotide renders the tumor cells more susceptible to eradication upon exposure to the hydroxyl radical up-regulator administered substantially concomitantly with or subsequent to administration of the oligonucleotide. This novel treatment, preferentially inhibits the proliferation or kills malignant cells but not normal cells. Preferably, the oligonucleotide is antisense to the gene which encodes protein p53, although other antisense oligonucleotides can also be used. The invention also includes novel conjugates of the oligonucleotide and the hydroxyl up-regulator, as well as new oligonucleotides.

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US PAT NO: 5,518,888 [IMAGE AVAILABLE] L38: 9 of 9

ABSTRACT:
Conjugated compounds which comprises an ST receptor binding moiety and a radiostable active moiety are disclosed. Pharmaceutical compositions comprising a pharmaceutically acceptable carrier or diluent, and a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radioactive active moiety are disclosed. Methods of treating an individual suspected of suffering from metastasized colorectal cancer comprising the steps of administering to said individual a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent, and a therapeutically effective amount of a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radiostable active moiety are disclosed. Methods of radioimaging metastasized colorectal cancer cells comprising the steps of first administering to an individual suspected of

having metastasized colorectal cancer cells, a pharmaceutical composition that comprises a pharmaceutically acceptable carrier or diluent, and conjugated compound that comprises an ST receptor binding moiety and a radioactive active moiety wherein the conjugated compound is present in an amount effective for diagnostic use in humans suffering from colorectal cancer and then detecting the localization and accumulation of radioactivity in the individual's body are disclosed.

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US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9
DATE ISSUED: Jul. 14, 1998
TITLE: Compositions and methods useful for inhibiting cell death and for delivering an agent into a cell
INVENTOR: Ban An Khaw, Milton, MA
Vladmir P. Torchilin, Charlestown, MA
Jagat Narula, Brookline, MA
Imran Vural, Brookline, MA
ASSIGNEE: Northeastern University, Boston, MA (U.S. corp.)
APPL-NO: 08/427,676
DATE FILED: Apr. 24, 1995
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Weingarten, Schurgin, Gagnebin & Hayes LLP

US PAT NO: 5,696,109 [IMAGE AVAILABLE] L38: 7 of 9
DATE ISSUED: Dec. 9, 1997
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INVENTOR: Bernard Malfroy-Camine, Arlington, MA
Susan Robin Doctrow, Roslindale, MA
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APPL-NO: 08/485,489
DATE FILED: Jun. 7, 1995
ART-UNIT: 125
PRIM-EXMR: William R. A. Jarvis
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US PAT NO: 5,641,754 [IMAGE AVAILABLE] L38: 8 of 9
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APPL-NO: 08/179,655
DATE FILED: Jan. 10, 1994
ART-UNIT: 189
PRIM-EXMR: John LeGuyader
LEGAL-REP: Zarley, McKee, Thomte, Voorhees & Sease

US PAT NO: 5,518,888 [IMAGE AVAILABLE] L38: 9 of 9
DATE ISSUED: May 21, 1996
TITLE: ST receptor binding compounds and methods of using the same
INVENTOR: Scott A. Waldman, Ardmore, PA
ASSIGNEE: Thomas Jefferson University, Philadelphia, PA (U.S. corp.)
APPL-NO: 08/141,892
DATE FILED: Oct. 26, 1993
ART-UNIT: 182

PRIM-EXMR: Toni R. Scheiner
ASST-EXMR: Lora M. Green
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris

=> d l38 bib ab 6,7,8

US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9
DATE ISSUED: Jul. 14, 1998
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APPL-NO: 08/427,676
DATE FILED: Apr. 24, 1995
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Weingarten, Schurgin, Gagnebin & Hayes LLP

US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9

ABSTRACT:
The invention relates to methods of salvaging a target cell from cell death, comprising contacting a target cell having a disrupted cell membrane with a specific affinity reagent-liposome conjugate in an amount effective and for a time sufficient to allow the conjugate to prevent cell death due to membrane disruption; and determining the viability of the target cell. Methods of delivering a selected agent into a damaged target cell for diagnosis and therapy are also disclosed.

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US PAT NO: 5,696,109 [IMAGE AVAILABLE] L38: 7 of 9

ABSTRACT:
The invention provides antioxidant salen-metal complexes, compositions of such antioxidant salen-metal complexes having superoxide activity, catalase activity, and/or peroxidase activity, compositions of salen-metal complexes in a form suitable for pharmaceutical administration to treat a disease associated with cell or **tissue** damage produced by free radicals such as superoxide, and cosmetic and free radical quenching formulations of salen metal compounds.

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INVENTOR: Patrick L. Iversen, Omaha, NE

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APPL-NO: 08/179,655
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US PAT NO: 5,641,754 [IMAGE AVAILABLE] L38: 8 of 9

ABSTRACT:
The present invention relates to methods and compositions for the treatment of cancer using an oligonucleotide and an hydroxyl radical up-regulator. The oligonucleotide is characterized by its ability to down-regulate the path by which the cell repairs oxidative damage to its DNA. Thus, the oligonucleotide renders the tumor cells more susceptible to eradication upon exposure to the hydroxyl radical up-regulator administered substantially concomitantly with or subsequent to administration of the oligonucleotide. This novel treatment, preferentially inhibits the proliferation or kills malignant cells but not normal cells. Preferably, the oligonucleotide is antisense to the gene which encodes protein p53, although other antisense oligonucleotides can also be used. The invention also includes novel conjugates of the oligonucleotide and the hydroxyl up-regulator, as well as new oligonucleotides.

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US PAT NO: 5,780,052 [IMAGE AVAILABLE] L38: 6 of 9

SUMMARY:

BSUM(6)

Delivery of drugs using liposomes allows for noninvasive treatment of diseases. Targeting of an organ or **tissue** type may be made more efficient using immunoliposomes, i.e., liposomes which are conjugated to an antibody specific for an organ-specific or **tissue**-specific antigen. Thus, one approach to targeted drug delivery is the use of drug-laden liposomes that have been made target-specific by. . .

SUMMARY:

BSUM(12)

Thus, the second aspect involves a method of delivering a **liposome-encapsulated** biological agent or nucleic acid to a **tissue** containing both healthy cells and membrane-disrupted cells, the membrane disruption either existing naturally or having been induced specifically. The method includes contacting the **tissue** with an effective amount of a specific affinity reagent-**liposome** conjugate containing the biological agent or nucleic acid and targeted to membrane-disrupted cells of the **tissue**. Contact of the conjugate with the target cells results in delivery of the agent to the cells of the **tissue** and restoration of the integrity of the cell membrane.

SUMMARY:

BSUM(13)

In . . . antibody, and the antibody may be specific for and bind to an intracellular antigen such as a cytoskeletal antigen. The **tissue** may comprise cardiac **tissue**, and the antibody may thus be specific for an intracellular antigen of cardiac **tissue**. The **tissue** may be

cancerous or normal.

SUMMARY:

BSUM(14)

The invention also features methods of inhibiting cell death in cardiac **tissue**, comprising providing cardiac **tissue** containing cardiomyocytes having intracellular myosin exposed at the cell exterior; contacting the cardiomyocytes with a conjugate comprising an immunoliposome comprising. . . a time sufficient to allow the conjugate to adhere to the cardiomyocyte; and determining the viability of cells of the **tissue**. Preferably, the intracellular antigen comprises myosin.

SUMMARY:

BSUM(17)

Preferably, the antineoplastic agent is selected from the group consisting of cytotoxic **agents**, toxins, **radiosensitizing** compounds, alpha-emitting radionuclides, beta-emitting radionuclides, antiproliferative agents and genes (for cytokines such as IL-2 and TNF). Preferably, the cells are. . .

SUMMARY:

BSUM(18)

As . . . or molecule than for a non-target substance or molecule. As used herein, the term includes antibodies specific for certain organs, **tissues**, cells, or cellular antigens, particularly intracellular antigens, and also includes ligands for which an internal cellular receptor exists.

SUMMARY:

BSUM(19)

In . . . not to antigens released into the general circulation upon cell death or to antigen on the exterior of living cells. **"Tissue"** refers to an agglomeration of cells that live in contact with each other in vivo, and may refer to both normal and abnormal **tissues**, including tumors, cancers, precancers, and neoplasms.

SUMMARY:

BSUM(26)

A . . . both therapeutic agents and effector molecules. A "therapeutic agent" refers to, e.g., antineoplastic agents and other pharmaceuticals and genes (for **tissue** transformation or differentiation). An "effector molecule" refers to, e.g., cytotoxic molecules, radionuclides, imaging agents, reporter groups, etiologic agents of infectious. . .

SUMMARY:

BSUM(27)

An . . . be considered an effective amount. Alternatively, where a drug or gene is desired to be delivered to a target cell, **tissue** or organ, an amount of the drug or gene is loaded into an immunoliposome and an amount of loaded immunoliposome. . .

DETDESC:

DETD(4)

Necrosis . . . death in an organ of the body may be the result of ischemic, inflammatory, immunologic and/or toxic insult to the **tissue**. Depending upon the location and severity of cell death, the consequences may be benign or significant enough to result in. . .

DETDESC:

DETD(38)

Loading of compounds into **liposomes** may be achieved by one or more of a variety of active and passive methods. Passive loading by entrapment is. . . a high efficiency in a target cell. It has been found for certain hydrophobic drugs, that the highest concentration of **encapsulated** material which can be achieved by passive loading is limited by their low intrinsic water solubility. The concentration of hydrophobic drug that can be accommodated in the **liposome** will depend on drug/lipid interactions in the membrane, but is generally limited to a drug concentration of less than about. . .

DETDESC:

DETD(47)

Antigens . . . cells, and spleen cells. The antigens include intracellular antigens, and antigens which are more available for binding when a cell, **tissue**, or organ is in a diseased or unhealthy state than in a healthy state. Intracellular cytoskeletal antigens will be particularly. . .

DETDESC:

DETD(69)

The . . . not on the cell wall. Myosin-specific antibodies have been developed and have been labeled for in vivo imaging of heart **tissue** damaged by myocardial infarction. (See, Khaw et al., J. Clin. Invest. 58:439, 1976).

DETDESC:

DETD(70)

Cardiac . . . days, as required. Administration of myosin-specific immunoliposomes may be especially useful, e.g, during reperfusion therapy to off-set the injury to **tissue** that occurs during such therapy. Therapeutic immunoliposomes may also be delivered by intracoronary infusion directly into the region at risk. . .

DETDESC:

DETD(72)

Therapeutic agents which may be **encapsulated** and thus used according to the invention for delivery to a target cell are presented in Table I. Table I. . . of representative useful agents and is not meant to be exhaustive. Generally, any therapeutic agent that is encapsulatable in a **liposome** and is therapeutically effective when used for targeted delivery is encompassed by the inventive methods. Also, as presented in Table. . .

DETDESC:

DETD(74)

A . . . the present invention. In addition to the above-listed agents, antineoplastic agents may include folate inhibitors, pyrimidine analogs, purine analogs, alkylating **agents**, antibiotics, and **radiosensitizing** compounds. Specific examples of such antineoplastic agents include acivicin, aclarubicin, acodazole, adriamycin, ametantrone, aminoglutethimide, anthramycin, asparaginase, azacitidine, azetepa, bisantrene, bleomycin,. . .

DETDESC:

DETD(83)

2. Local depot delivery: Immunoliposomes using intracellular targets of irreversibly injured cells as anchors for gene delivery to surrounding **tissues**.

DETDESC:

DETD(85)

For . . . Thus, the mode of DNA delivery according to the invention provides noninvasive and effective delivery to a partially damaged target **tissue**.

DETDESC:

DETD(88)

Modern techniques for nonsurgical treatment of cancer include both clinical and experimental techniques involving chemotherapy, **radiation therapy**, a combination of chemotherapy and **radiation therapy**, and immunotherapy. In each instance, the object of the therapy is to kill the malignant cells. Antineoplastic agents presently or. . .

DETDESC:

DETD(92)

One diagnostic procedure of the present invention involves diagnosing sites of necrosis in an organ or **tissue**. This procedure utilizes immunoliposomes specific for intracellular antigens and containing a diagnostic agent, e.g., a detectable molecule such as an. . . discussed. The radionuclide may be attached to a convenient carrier molecule, such as a chelating polymer. The radionuclide-containing immunoliposome is **injected** (preferably intravenously) into a patient suspected of containing an organ or **tissue** that is undergoing cell death; for example, a patient who has received chemotherapy, **radiation therapy**, or both. This procedure is preferably carried out at least one or two days after the initiation of the therapy, in order to permit resultant necrosis of the neoplastic **tissue** to advance to a sufficient point that reasonable numbers of necrotic cells are present. Between 30 minutes and 3 days following **administration** of the labeled antibody, an appropriate scintigraphic imaging technique is employed to image the label that is localized in necrotic **tissue**. Suitable imaging techniques include gamma cameras and SPECT (single photon emission computed tomography) techniques.

DETDESC:

DETD(93)

One . . . intracellular antigen that has been labeled with a radiopaque material is injected a suitable time after initiation of chemotherapy or **radiation therapy**. After the antibody has localized at the areas of necrotic **tissue**, radiographic imaging is performed. Other suitable techniques include CAT (computed axial tomography) scans, fluoroscopy and conventional **X-ray** imaging.

DETDESC:

DETD(96)

In the augmentation approach, tumor necrosis is initiated by any conventional technique, such as chemotherapy, immunotherapy, **radiation therapy**, or the like.

DETDESC:

DETD(97)

After . . . at least two days after initiation of the primary therapy), immunoliposomes containing the therapeutic compound, preferably an antineoplastic agent, are **administered** to the patient. Intravenous **administration** is preferred, although direct **injection** in the vicinity of the tumor is also contemplated.

DETDESC:

DETD(99)

If . . . way, a diffusion effect may be possible with destruction of the tumor cells proceeding radially from necrotic to healthy tumor **tissue**. To achieve this diffusion effect, a cytotoxic agent such as a beta-emitting or an alpha-emitting radionuclide may be used.

DETDESC:

DETD(117)

Mongrel . . . Natick, Mass.). The right femoral artery and vein are isolated and catheterized to facilitate monitoring of arterial pressures and the **administration** of medication. Arterial pressure and a multilead electrocardiogram are continuously monitored. A left thoracotomy is performed, and the heart is. . . diagonal branch. A small branch just distal to the site of occlusion is cannulated with a 22-gauge catheter for the **administration** of antimyosin immunoliposomes into the LAD. The LAD is occluded by tightening the snare, and a prophylactic lidocaine infusion of. . . receive the same volume of intracoronary saline. The animals are killed at 24 hours or 7 days later by atrial **injection** of 20 to 40 mEq of potassium chloride for histolochemical and histological characterization of the infarcted myocardium. The heart is. . .

DETDESC:

DETD(118)

Cell membrane sealing is assessed by survival/viability testing of **tissue**, using nitroblue tetrazolium staining. Alternatively, to demonstrate liposome sealing of injured cells, fluorescein-labeled phospholipids are used in the preparation of. . .

DETDESC:

DETD(126)

The . . . described (Khaw et al., J. Nucl. Med. 28:76-82, 1987). The pixel size is calibrated, and the absolute volume of infarcted **tissue** is determined (area.times.slice thickness). This value, multiplied by the specific gravity of myocardium (1.05), is used to determine the weight of the infarcted **tissue** in grams (Ostrzega et al., Am. Heart J. 117:444-452, 1989). The percent infarct relative to the ventricular mass is then. . .

DETDESC:

DETD(130)

Immunoliposomes administered according to the invention are administered intravenously, intraperitoneally or directly to the target **tissue** or organ, at a dosage that is appropriate for the amount of biological agent or genetic material that is **encapsulated** by the **liposome**. Immunoliposome dosage will therefore vary from about 5 mg/kg body weight to about 1 gm/kg body weight, and may be. . .

CLAIMS:

CLMS(1)

What is claimed is:

1. A method of inhibiting cell death in cardiac **tissue**, said method comprising
providing cardiac **tissue** comprising injured cardiomyocytes having intracellular myosin exposed to the exterior of said cardiomyocytes;
contacting said injured cardiomyocytes with a specific affinity. . .

US PAT NO: 5,696,109 [IMAGE AVAILABLE] L38: 7 of 9

ABSTRACT:
The . . . activity, compositions of salen-metal complexes in a form suitable for pharmaceutical administration to treat a disease associated with cell or **tissue** damage produced by free radicals such as superoxide, and cosmetic and free radical quenching formulations of salen metal compounds.

SUMMARY:

BSUM(2)

The . . . antioxidants as preservatives and oxyradical quenching agents in hydrocarbons, methods for using the small molecule antioxidants for targeted protection of **tissues** and/or cell types during cancer chemotherapy, and methods for using the small molecule antioxidants to prevent toxicologic damage to individuals. . . are also used for preventing oxidative damage in human transplant organs and for inhibiting reoxygenation injury following reperfusion of ischemic **tissues**. The compositions and methods of the invention are also useful for chemoprevention of chemical carcinogenesis and alteration of drug metabolism. . .

SUMMARY:

BSUM(6)

Biological . . . acid, and metal-binding proteins. Various antioxidants, being both lipid and water soluble, are found in all parts of cells and **tissues**, although each specific antioxidant often shows a characteristic distribution pattern. The so-called ovothiols, which are mercaptohistidine derivatives, also decompose peroxides. . .

SUMMARY:

BSUM(7)

Free . . . and other disease. Oxyradicals can react with proteins, nucleic acids, lipids, and other biological macromolecules producing damage to cells and **tissues**, particularly in the critically ill patient.

SUMMARY:

BSUM(9)

Free . . . cytochrome P-450-catalyzed monooxygenation reactions of drugs and xenobiotics (e.g., trichloromethyl radicals, CCl.sub.3 .cndot., formed from oxidation of carbon tetrachloride), and **ionizing radiation**. For example, when **tissues** are exposed to gamma radiation, most of the energy deposited in the cells is absorbed by water and results in. . . radical, which is believed to be an essential factor in producing the cytotoxic effect of activated neutrophils. Reperfusion of ischemic **tissues** also produces large concentrations of oxyradicals, typically superoxide (Gutteridge J. M. C. and Halliwell B. (1990) Arch. Biochem. Biophys. 283:. . .

SUMMARY:

BSUM(10)

Oxygen, . . . the neutrophil "respiratory burst", superoxide anion is generated by the membrane-bound NADPH oxidase. ROS are also believed to accumulate when **tissues** are subjected to ischemia followed by reperfusion.

SUMMARY:

BSUM(22)

In an effort to prevent the damaging effects of oxyradical formation during reoxygenation of ischemic **tissues**, a variety of antioxidants have been used.

SUMMARY:

BSUM(28)

Based . . . inexpensive to manufacture, stable, and possess advantageous pharmacokinetic properties, such as the ability to cross the blood-brain barrier and penetrate **tissues**. Such versatile antioxidants would find use as pharmaceuticals, chemoprotectants, and possibly as dietary supplements. It is one object of the. . .

SUMMARY:

BSUM(29)

It . . . isoprene rubbers, other rubber analogs, oils and waxes, cosmetic bases, animal fats, petroleum and petrochemicals and distillates, polymerizable resins, dyes, **photosensitive agents**, flavor **agents**, adhesives, sealants, polymer precursors, and the like. Also encompassed in the invention are salen-metal antioxidants and methods for inhibiting oxyradical-mediated. . .

SUMMARY:

BSUM(33)

The . . . are typically salen-manganese complexes, such as Mn(III)-salen complexes. The invention provides methods for preventing or reducing ischemic/reperfusion damage to critical **tissues** such as the myocardium and central nervous system. The invention also provides methods for preventing or reducing cellular damage resulting. . .

SUMMARY:

BSUM(34)

In . . . (2) for preserving organs for transplant in an anoxic, hypoxic, or hyperoxic state prior to transplant, (3) for protecting normal **tissues** from free radical-induced damage consequent to exposure to **ionizing radiation** and/or chemotherapy, as with bleomycin, (4) for protecting cells and **tissues** from free radical-induced injury consequent to exposure to xenobiotic compounds which form free radicals, either directly or as a consequence of monooxygenation through the cytochrome P-450 system, (5) for enhancing cryopreservation of cells, **tissues**, organs, and organisms by increasing viability of recovered specimens, and (6) for prophylactic administration to prevent: carcinogenesis, cellular senescence, cataract. . .

SUMMARY:

BSUM(36)

In . . . the invention at a concentration of at least 1 nM but not more than about 100 mM is formulated for **administration**, usually at a concentration of about 0.1 to 10 mM, typically by intravenous route, to a patient undergoing or expected. . . antineoplastic or antihelminthic chemotherapy employing a chemotherapeutic agent which generates free radicals, (3) endotoxic shock or sepsis, (4) exposure to **ionizing radiation**, (5) exposure to exogenous chemical compounds which are free radicals or produce free radicals, (6) thermal or chemical burns or. . . and myocardial irrigation. Nonaqueous formulations, such as lipid-based formulations are also provided, including stabilized emulsions. The antioxidant salen-metal compositions are **administered** by various routes, including intravenous **injection**, intramuscular **injection**, subdermal **injection**, intrapericardial **injection**, surgical irrigation, topical application, ophthalmologic application, lavage, gavage, enema, intraperitoneal infusion, mist inhalation, oral rinse, and other routes, depending upon. . .

SUMMARY:

BSUM(44)

The . . . may be effected by means other than those listed herein. Further, the peroxide-induced condition may involve cataracts, inflammation of a **tissue**, ischemia, an allergic reaction, or pathology caused by oxidative stress. Where the peroxide-induced condition involves cataracts, administration is effected by,. . .

DETDESC:

DETD(6)

The . . . method is used for preventing, arresting, or treating (1) neurological damage such as Parkinson's disease or anoxia injury, (2) cardiac **tissue** necrosis resulting from cardiac ischemia, (3) autoimmune neurodegeneration (e.g., encephalitis), (4) acute lung injury such as in sepsis and endotoxemia,. . .

DETDESC:

DETD(66)

The compositions for parenteral **administration** will commonly comprise a solution of an antioxidant salen-transition metal complex or a cocktail thereof dissolved in an acceptable carrier,. . . 100 mM and will be selected primarily based on fluid volumes, viscosities, etc., in accordance with the particular mode of **administration** selected. Most usually, the antioxidant salen-metal complex is present at a concentration of 0.1 mM to 10 mM. For example, a typical formulation for intravenous **injection** comprises a sterile solution of an antioxidant salen-metal complex (e.g., C7) at a concentration of 5 mM in Ringer's solution.. . . aqueous vehicle comprising a detergent or other lipophilic agent (e.g., Tween, NP-40, PEG); alternatively, the antioxidant salen complexes may be **administered** as a suspension in an aqueous carrier, or as an emulsion.

DETDESC:

DETD(67)

Thus, a typical pharmaceutical composition for intramuscular **injection** could be made up to contain 1 ml sterile buffered water, and about 1-100 mg of antioxidant salen-transition metal complex(es).. . . antioxidant salen-transition metal complex(es). Lipophilic agents may be included in formulations of lipophilic salen-metal complexes. Actual methods for preparing parenterally **administrable** compositions will be known or apparent to those skilled in the art and are described in more detail in, for. . .

DETDESC:

DETD(69)

The compositions containing the present antioxidant salen-transition metal complex(es) or cocktails thereof can be **administered** for prophylactic and/or therapeutic treatments. In therapeutic application, compositions are **administered** to a patient already affected by the particular free radical-associated disease, in an amount sufficient to cure or at least. . . this use will depend upon the severity of the condition, the general state of the patient, and the route of **administration**, but generally range from about 1 mg to about 10 g of antioxidant salen-transition metal complex(es) per dose, with dosages. . . treating acute myocardial ischemia/reoxygenation episodes, about 100 to 1000 mg of a antioxidant salen metal complex (e.g., C7) may be **administered** systemically by intravenous infusion; at least about 10 mg to 500 mg of antioxidant salen-metal complex(es) may be **administered** by intrapericardial **injection** to provide elevated local concentrations of SOD activity in the myocardium.

DETDESC:

DETD(74)

The dosage of SOD-mimetic salen-metal complex(es) will vary with each particular application. Typically, the composition is **administered** either systemically or topically. Systemic **administration** includes per os and parenteral routes; topical **administration** includes in situ applications. The in situ means includes, for example, **administering** an SOD-mimetic salen-metal complex by endoscopic bolus wash and/or paravenous **injection**, or in the case of lower GI treatments, by enema. Parenteral routes may include, for example, subcutaneous, intradermal, intramuscular, and. . . salen-metal complex(es) will range from about 2 to 5,000 mg or more, typically 10 to 1000 mg,

depending on the **administration** interval and route, which can range from a single oral dose, parenteral dose and/or topical dose to multiple oral doses,. . .

DETDESC:

DETD(78)

According . . . the group consisting of: N-2-mercaptopropionylglycine, N-acetylcysteine, glutathione, dimethyl thiourea, desferrioxamine, mannitol, .alpha.-tocopherol, ascorbate, allopurinol, 21-aminosteroids, calpain inhibitors, glutamate receptor antagonists, **tissue** plasminogen activator, streptokinase, urokinase, nonsteroidal anti-inflammatory agent, cortisone, and carotenoids. Antioxidant salen-Mn complexes may also be administered in conjunction with. . .

DETDESC:

DETD(83)

The . . . include, for example, solid, semi-solid and liquid dosage forms, such as tablets, pills, powders, liquid solutions or suspensions, liposome preparations, **injectable** and infusible solutions. The preferred form depends on the intended mode of **administration** and therapeutic application. Typically, a sterile solution of a salen-metal complex in an aqueous solvent (e.g., saline) will be **administered** intravenously. The compositions also preferably include conventional pharmaceutically acceptable carriers and adjuvants which are known to those of skill in the art. See, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Co.: Easton, Pa., 17th Ed. (1985). Generally, **administration** will be by oral or parenteral (including subcutaneous, intramuscular, intravenous, and intradermal) routes, or by topical application or infusion into a body cavity, or as a bathing solution for **tissues** during surgery.

DETDESC:

DETD(92)

Parenteral **administration** is generally characterized by **injection**, either subcutaneously, intramuscularly or intravenously. **Injectables** can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to **injection**, or as emulsions. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol or the like. In addition, if desired, the pharmaceutical compositions to be **administered** may also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents and the. . .

DETDESC:

DETD(96)

Antioxidant salen-metal complex(es) can also be added to rinse or storage solutions for organs and **tissues**, such as for organ transplantation or for surgical rinses. For example, excised organs are often placed in a preservation solution. . .

DETDESC:

DETD(97)

Typically . . . salen-metal complex can be used to provide enhanced

storage or irrigation of organs (e.g., kidney, liver, pancreas, lung, fetal neural **tissue**, heart, vascular grafts, bone, ligament, tendon, skin) which is believed to enhance the viability of the **tissue** and increase resistance to oxidative damage (e.g., as a consequence of ischemia/reperfusion).

DETDESC:

DETD(99)

Alternatively, . . . to catalyze the decomposition of reactive oxygen species can be used to advantage to inhibit or slow damage to biological **tissues** and cells. For example, benzoyl peroxide is a widely used treatment for acne lesions; excessive or inappropriate application of benzoyl. . . treated by local (or if desired, systemic) administration of an antioxidant salen-metal complex (e.g., C7). Similarly, oxyradical-induced damage to connective **tissues** (e.g., collagen) attendant to exposure to UV light, cigarette smoking, and senescence may be reduced by administration of an antioxidant. . .

DETDESC:

DETD(101)

Antioxidant salen-transition metal complexes, typically antioxidant salen-Mn complexes, such as compound C7, are used to protect cells and **tissues** from free radical-producing agents, such as **ionizing radiation** and chemotherapeutic agents (e.g., bleomycin). Preferably, a protective dosage comprising at least about 1 .mu.g of salen-Mn complex/kg bodyweight is **administered** by one or more of several routes (e.g., oral, intraveneous, intraperitoneal, intragastric lavage, enema, portal vein infusion, topical, or inhalation of mist), preferably by **injection** of liposomes or immunoliposomes for targeted delivery of the antioxidant salen-Mn complexes to protect normal cells, for example, against free. . . of commencement, and preferably within about 3-6 hours of commencement of the chemotherapy and/or radiotherapy. Antioxidant salen-Mn may be continually **administered** to the patient during the course of therapy.

DETDESC:

DETD(102)

For example, a solution of an antioxidant salen-metal complex can be **encapsulated** in **micelles** to form immunoliposomes (U.S. Pat. No. 5,043,164, U.S. Pat. No. 4,957,735, U.S. Pat. No. 4,925,661; Connor and Huang (1985) J.. . .

DETDESC:

DETD(109)

In . . . anti-inflammatory agent in a cosmetic base or dental linament (periodontal disease) for topical application for local prevention of inflammation and/or **tissue** damage consequent to inflammation. A variety of steroidal and non-steroidal anti-inflammatory agents can be combined with an antioxidant salen-metal compound.

DETDESC:

DETD(162)

Rats received an intramuscular **injection** of 0.25 ml of an iron-dextran solution (100 g iron hydroxide, 99 g dextran, water up to 11) every third day during a 5-week period to achieve a significant iron

overload in cardiac **tissue**. At the end of this treatment, rats were anesthetized with sodium pentobarbital (40 mg/kg) and heparin (1,000 IU/kg) was **administered** via a femoral vein. Hearts were then removed and rapidly perfused through the aorta according to the technique described by. . .

DETDESC:

DETD(188)

All . . . post-mortem. Lung lipid peroxidation was estimated fluorometrically by measuring thiobarbituric acid reactive products in the lipid fraction of lung parenchymal **tissue** harvested at T=300 min.

DETDESC:

DETD(203)

MPTP in mice. Adult male CFW mice (25-33 g) were **administered** two **injections** of MPTP dissolved in normal saline (40 mg/kg, s.c.) 24 hours apart. A group of animals also received C7 in three **injections** (33 mg/kg, s.c.) **administered** 24 hours apart, starting 1 day before the onset of MPTP treatment. Animals were sacrificed 7 days after the first MPTP **injection**, and neuronal pathology was assessed by the binding of .sup.3 H-mazindol, a ligand for the dopamine transporter, to 10 mm. . .

DETDESC:

DETD(218)

Synthetic catalytic scavengers of reactive oxygen species (ROS) may have clinical value in alleviating **tissue** damage associated with numerous acute and chronic diseases. Example 1 demonstrates that synthetic salen manganese complexes have superoxide dismutase (SOD) activity. One of these compounds, C7, has been found to be protective in several models for ROS-associated **tissue** injury. In this example, the catalytic properties of C7, in particular, are further characterized demonstrating that it also utilizes hydrogen. . .

DETDESC:

DETD(223)

0-Vanillin, . . . purchased from EM Sciences (Gibbstown, N.J.). The XTT reagent was obtained from Boehringer Mannheim, Inc. (Indianapolis, Ind.). All components of **tissue** culture media were purchased from BioWhittaker (Walkersville, Md.) and **tissue** culture plastic ware was from Corning (Corning, N.Y.). All other chemicals were obtained from Sigma Chemicals (St. Louis, Mo.).

DETDESC:

DETD(237)

Human dermal fibroblasts (HF cells) were obtained from the American type **tissue** Culture Collection at passage 1 and cultured and propagated in a medium (HF medium) consisting of Dulbecco's Modified Eagle's Medium. . . incubated with HF medium containing glucose oxidase (0.019 units/ml) along with test compounds, as indicated, for 18 hr in the **tissue** culture incubator. Fresh HF medium was then added and cell viability assessed using the XTT reagent as described above. For. . .

DETDESC:

DETD(256)

In **tissues**, ROS promote **tissue** destruction in part through oxidative damage to cellular macromolecules, in particular, by inducing lipid peroxidation. The salen manganese compounds were tested for the ability to protect brain **tissue** from lipid peroxidation induced by incubating brain homogenates with iron in an oxygen-rich atmosphere. Malonyldialdehyde, a byproduct of lipid peroxidation,. . .

DETDESC:

DETD(259)

Salen . . . cells due to its intracellular decomposition to alkoxyl and methoxyl free radicals. It has been reported that SOD, particularly when **encapsulated** into **liposomes**, protects hepatocytes from t-BHP toxicity, implying that intracellular superoxide may play a role in the cytotoxicity of this organic hydroperoxide.. . .

DETDESC:

DETD(266)

The . . . pathology. In Example 1, C7 has already been shown to be protective in much more complex biological models for ROS-induced **tissue** damage than those employed in Example 2.

CLAIMS:

CLMS(6)

6. . . . wherein the free radical-associated disease state is: neurological damage from Parkinson's disease, Alzheimer's disease or transient cerebral anoxia injury, cardiac **tissue** necrosis resulting from cardiac ischemia, autoimmune neurodegeneration, acute lung injury from sepsis and/or endotoxemia, neuronal damage resulting from anoxia or. . .

CLAIMS:

CLMS(9)

9. A method for treating cardiac **tissue** necrosis resulting from cardiac ischemia or acute lung injury from sepsis or endotoxemia, neuronal damage resulting from anoxia, or iatrogenic. . .

US PAT NO: 5,641,754 [IMAGE AVAILABLE] L38: 8 of 9

SUMMARY:

BSUM(8)

Hydroxy radicals, in particular, are extremely reactive and represent the most active mutagen derived from **ionizing radiation**. The radical is highly electrophilic and reactive, with a capacity to bind to DNA to produce modified bases, such as 8-hydroxyguanine, and thymine glycol. The former has been detected in DNA isolated from **tissues** exposed to **ionizing radiation** or to hydrogen peroxide (H.sub.2 O.sub.2) (Kasai et al., Carcinogenesis 7: 1849, 1986). The latter, which is an oxidation product. . .

SUMMARY:

BSUM(14)

Other . . . E (alpha-tocopherol); Vitamin C (ascorbic acid); and the trace mineral element selenium, all of which serve in a variety of **tissues** and bodily processes as general reducing agents.

SUMMARY:

BSUM(15)

Cancer . . . notably deficient in the scavenger protection systems discussed above. Because of this fact, irradiation kills cancer cells preferentially to normal **tissue** and conventional **radiation therapy** attempts to exploit this mechanism of action, as do certain conventional chemotherapeutic agents, such as the nitrosoureas, e.g., BCNU (bis-chloroethylnitrosourea),. . .

SUMMARY:

BSUM(16)

However, the sensitivity of a cell and the resultant cellular response to **ionizing radiation** depends primarily on the presence or absence of oxygen within the cell and upon the stage of division which the cell is in at the time of irradiation. In **radiation therapy**, production of oxidative damage is initiated by a dose of radiation. Cells which are oxygen-rich and sensitive to radiation will. . .

SUMMARY:

BSUM(23)

Thus, . . . increased dramatically, leading to delayed p53 independent apoptosis of the targeted cells with little or no adverse effect on normal **tissue** (as normal **tissue** has greater oxygen scavenging activity).

SUMMARY:

BSUM(25)

The agent capable of radical oxygen induced cytotoxicity can be, for example, a **radiosensitizer**, a chemotherapeutic **agent** which generates radical oxygen, or any oligonucleotide capable of interaction with cells of the host causing the formation of hydroxy. . . by one or more sensitizing agents, may be used in the method of the invention. Included are radiation (whether the **radiation therapy** is delivered internally or administered by external means) and cytotoxic drugs. Examples of some of the many such drugs are. . .

SUMMARY:

BSUM(26)

Internally delivered radiation includes therapeutically effective radioisotopes **injected** into a patient. Such radioisotopes include, but are not limited to, the radionuclide metals .sup.186 Re, .sup.188 Re, .sup.64 Cu,. . . I. These radioisotopes generally will be bound to carrier molecules (e.g., are in the form of a chelate-antibody conjugate) when **administered** to a patient. Examples of suitable internally delivered radiotherapeutic agents are the metal radionuclide chelates which are conjugated to antibodies as described in European Patent Application Publication No. 188,256. Radiation **administered** by external means includes external beam radiation such as cobalt therapy.

DETDESC:

DETD(2)

The . . . for selectively inducing apoptosis by enhancing the action of hydroxy radicals against the DNA of a particular type of target **tissue** compared to non-target **tissue**. The method comprises administering to a mammalian or human host a sensitizing agent and an oligonucleotide, either separately or concomitantly,. . .

DETDESC:

DETD(5)

The . . . may be an oligonucleotide antisense to any of the mRNA of any of the oxygen radical scavenger proteins, a chemotherapeutic **agent**, or **radiosensitizer**, such as BSO, or any compound which will increase the amount of hydroxy radicals in the cell.

DETDESC:

DETD(34)

To . . . young (4-6 week old) BDF1 mice supplied by Jackson Laboratories, Bar Harbor, Me. The mice were humanely euthanized, and thymic **tissue** removed and minced. A cell suspension was prepared by repeated gently aspiration of the cells into a 1 ml syringe. . .

DETDESC:

DETD(58)

Suitable formulations for parenteral **administration** include aqueous solutions of the active compounds in water-soluble or water-dispersible form. In addition, suspensions of the active compounds as appropriate oily **injection** suspensions may be **administered**. Suitable lipophilic solvents or vehicles include fatty oils, for example, sesame oil, or synthetic fatty acid esters, for example, ethyl oleate or triglycerides. Aqueous **injection** suspensions may contain substances which increase the viscosity of the suspension include, for example, sodium carboxymethyl cellulose, sorbitol, and/or dextran,. . .

DETDESC:

DETD(59)

In . . . administered by a variety of specialized delivery techniques. For example, the compounds of the present invention may also be administered **encapsulated** in **liposomes**, pharmaceutical compositions wherein the active ingredient is contained either dispersed or variously present in corpuscles consisting of aqueous concentric layers. . . ionic surfactants such as diacetylphosphate, stearylamine, or phosphatidic acid, and/or other materials of a hydrophobic nature. The diameters of the **liposomes** generally range from about 15 nm to about 5 microns.

CLAIMS:

CLMS(5)

5. The method of claim 1 wherein the free radicals are produced by an effective amount of a **radiosensitizing agent**.

CLAIMS:

CLMS(7)

7. The method of claim 1 wherein the free radicals are produced by **ionizing radiation.**

CLAIMS:

CLMS(8)

8. The method of claim 5 wherein said **radiosensitizing agent** is an oxygen generator.

US PAT NO: 5,800,992 [IMAGE AVAILABLE] L41: 3 of 3
DATE ISSUED: Sep. 1, 1998
TITLE: Method of detecting nucleic acids
INVENTOR: Stephen P.A. Fodor, 3863 Nathan Way, Palo Alto, CA 94303
Dennis W. Solas, 50 Gardenside Dr., #13, San Francisco, CA 94131
William J. Dower, 761 Partridge Ave., Menlo Park, CA 94025
APPL-NO: 08/670,118
DATE FILED: Jun. 25, 1996
ART-UNIT: 164
PRIM-EXMR: Stephanie W. Zitomer

=> d l41 3 ab

US PAT NO: 5,800,992 [IMAGE AVAILABLE] L41: 3 of 3

ABSTRACT:
The present invention provides method and apparatus for sequencing, fingerprinting and mapping biological macromolecules, typically biological polymers. The methods make use of a plurality of sequence specific recognition reagents which can also be used for classification of biological samples, and to characterize their sources.

US PAT NO: 5,800,992 [IMAGE AVAILABLE] L41: 3 of 3

DETDESC:

DETD(82)

In . . . of the protection are described below and in related Pirrung et al. (1992)U.S. Pat. No. 5,143,854. In a preferred embodiment, **photosensitive** protecting **agents** will be used and the regions of activation or deactivation may be controlled by electro-optical and optical methods, similar to. . .

DETDESC:

DETD(86)

The . . . benzyloxy carbonyl, 5-bromo-7-nitroindolinyl, O-hydroxy-.alpha.-methyl cinnamoyl, and 2-oxymethylene anthraquinone. Examples of activators include ion beams, electric fields, magnetic fields, electron beams, **x-ray**, and other forms of electromagnetic radiation.

DETDESC:

DETD(113)
b. **Tissue** transplants

DETDESC:

DETD(255)

Besides . . . may be classified or characterized by analyzing the pattern of specific interaction. This may be applicable to a cell or **tissue** type, to the messenger RNA population expressed by a cell to the genetic content of a cell, or to virtually. . .

DETDESC:

DETD(299)

As . . . present invention is also useful in defining specific stages in the temporal sequence of cells, e.g., development, and the resulting **tissues** within an organism. For example, the developmental stage of a cell, or population of cells, can be dependent upon the. . .

DETDESC:

DETD(301)

In . . . circulating cells. Many of the cells for which this would be most useful will be immobile cells found in particular **tissues** or organs. Tumor cells will be diagnosed or detected using these fingerprinting techniques. Coupled with a temporal change in structure,. . .

DETDESC:

DETD(384)

A . . . 6-dimethylamino-1,2-benzophenazin; retinol; bis (3'-aminopyridinium) 1,10-decandiyl diiodide; sulfonaphthylhydrazone of hellibrienin; chlorotetracycline; N-(7-dimethylamino-4-methyl-2-oxo-3-chromenyl)maleimide; N-[p-(2-benzimidazolyl)-phenyl]maleimide; N-(4-fluoranthyl)maleimide; bis(homovanillic acid); resazarin; 4-chloro-7-nitro-2,1,3-benzooxadiazole; merocyanine 540; resorufin; **rose bengal**; and 2,4-diphenyl-3(2H)-furanone.

DETDESC:

DETD(614)

The . . . sequencing provides specific reagents useful for fingerprinting applications. Fingerprinting embodiments may be applied towards polynucleotide fingerprinting, polypeptide fingerprinting, cell and **tissue** classification, cell and **tissue** temporal development stage classification, diagnostic tests, forensic uses for individual identification, classification of organisms, and genetic screening of individuals. Mapping. . .

DETDESC:

DETD(626)

T-cell . . . may be defined. For example, different neural cell types may be defined on the basis of cell surface antigens. Different **tissue** types will be defined on the basis of **tissue** specific antigens. Developmental cell classes will be similarly defined. All of these screenings can make use of the VLSIPS substrates. . .

DETDESC:

DETD(669)

The . . . For example, in some embodiments it may be desirable to use protective groups which are sensitive to electron beam irradiation, **x-ray** irradiation, in combination with electron beam lithograph, or **x-ray** lithography techniques. Alternatively, the group could be removed by exposure to an electric current. The scope of the invention should, . . .

US PAT NO: 5,879,656 [IMAGE AVAILABLE] L38: 2 of 9
DATE ISSUED: Mar. 9, 1999
TITLE: Methods of treating metastatic colorectal cancer with ST receptor binding compounds
INVENTOR: Scott A. Waldman, Ardmore, PA
ASSIGNEE: Thomas Jefferson University, Philadelphia, PA (U.S. corp.)
APPL-NO: 08/583,447
DATE FILED: Jan. 5, 1996
ART-UNIT: 168
PRIM-EXMR: Lora M. Green
ASST-EXMR: Joseph W. Ricigliano
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris, LLP

US PAT NO: 5,879,656 [IMAGE AVAILABLE] L38: 2 of 9

ABSTRACT:
Conjugated compounds which comprises an ST receptor binding moiety and a radiostable active moiety are disclosed. Pharmaceutical compositions comprising a pharmaceutically acceptable carrier or diluent, and a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radioactive active moiety are disclosed. Methods of treating an individual suspected of suffering from metastasized colorectal cancer comprising the steps of administering to said individual a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent, and a therapeutically effective amount of a conjugated compound which comprises an ST receptor binding moiety and a radiostable active moiety or an ST receptor binding moiety and a radiostable active moiety are disclosed. Methods of radioimaging metastasized colorectal cancer cells comprising the steps of first administering to an individual suspected of having metastasized colorectal cancer cells, a pharmaceutical composition that comprises a pharmaceutically acceptable carrier or diluent, and conjugated compound that comprises an ST receptor binding moiety and a radioactive active moiety wherein the conjugated compound is present in an amount effective for diagnostic use in humans suffering from colorectal cancer and then detecting the localization and accumulation of radioactivity in the individual's body are disclosed.

US PAT NO: 5,840,276 [IMAGE AVAILABLE] L38: 3 of 9
DATE ISSUED: Nov. 24, 1998
TITLE: Activatable infusable dispersions containing drops of a superheated liquid for methods of therapy and diagnosis
INVENTOR: Robert E. Apfel, New Haven, CT
ASSIGNEE: Apfel Enterprises, Inc., New Haven, CT (U.S. corp.)
APPL-NO: 08/780,337
DATE FILED: Jan. 8, 1997
ART-UNIT: 166
PRIM-EXMR: Gary E. Hollinden
ASST-EXMR: Michael G. Hartley
LEGAL-REP: Fish & Richardson P.C.

US PAT NO: 5,840,276 [IMAGE AVAILABLE] L38: 3 of 9

ABSTRACT:
Dispersions of superheated drops of immiscible liquids in aqueous

continuous phase suitable for infusion into a human or other animal, the drops being vaporizable in a selected body location by **ionizing radiation** or ultrasound. The dispersions can be used to form diagnostic contrast agents, to improve diffusion of drugs, to occlude capillaries and to deliver drugs selectively in a localized body region.

US PAT NO: 5,827,880 [IMAGE AVAILABLE] L38: 5 of 9
DATE ISSUED: Oct. 27, 1998
TITLE: Synthetic catalytic free radical scavengers useful as antioxidants for prevention and therapy of disease
INVENTOR: Bernard Malfroy-Camine, Arlington, MA
Susan Robin Doctrow, Roslindale, MA
ASSIGNEE: Eukarion, Inc., Bedford, MA (U.S. corp.)
APPL-NO: 08/380,731
DATE FILED: Jan. 26, 1995
ART-UNIT: 124
PRIM-EXMR: Porfirio Nazario-Gonzalez
LEGAL-REP: Townsend and Townsend and Crew LLP

US PAT NO: 5,827,880 [IMAGE AVAILABLE] L38: 5 of 9

ABSTRACT:
The invention provides antioxidant salen-metal complexes, compositions of such antioxidant salen-metal complexes having superoxide activity, catalase activity, and/or peroxidase activity, compositions of salen-metal complexes in a form suitable for pharmaceutical administration to treat or prevent a disease associated with cell or **tissue** damage produced by free radicals such as superoxide, and cosmetic and free radical quenching formulations of salen metal compounds.

Structure search limits have been increased. See HELP SLIMIT
for details.

=> s rose bengal

```
           725 ROSE
            64 BENGAL
L2          36 ROSE BENGAL
                 (ROSE(W)BENGAL)
```

=> s rose bengal/cn

```
L3           1 ROSE BENGAL/CN
```

=> d

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN 11121-48-5 REGISTRY
CN **Rose Bengal (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Bengal Rose
CN Rose Bengale
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1775 REFERENCES IN FILE CA (1967 TO DATE)
77 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1779 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.12	27.89

FILE 'CAPLUS' ENTERED AT 15:11:25 ON 10 AUG 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1967 - 10 Aug 2000 VOL 133 ISS 7
FILE LAST UPDATED: 9 Aug 2000 (20000809/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

=> s l3 and cancer

```
          1779 L3
        117210 CANCER
         15739 CANCERS
        121823 CANCER
                  (CANCER OR CANCERS)
L4           2 L3 AND CANCER
```

=> d ibib abs hitstr 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:215766 CAPLUS
DOCUMENT NUMBER: 126:196947
TITLE: Modified fluorogenic substrates with enzyme-hydrolyzable quencher group for diagnosis and photodynamic treatment of tumors
INVENTOR(S): Bottiroli, Giovanni; Croce, Anna Cleta; Baglioni, Piero; Monici, Monica
PATENT ASSIGNEE(S): Consiglio Nazionale delle Ricerche, Italy; Bottiroli, Giovanni; Croce, Anna Cleta; Baglioni, Piero; Monici, Monica
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703697	A2	19970206	WO 1996-EP3201	19960719
WO 9703697	A3	19970410		

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,

IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2227212	AA	19970206	CA 1996-2227212	19960719
AU 9667351	A1	19970218	AU 1996-67351	19960719
EP 839051	A1	19980506	EP 1996-927559	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, IE				
US 6036941	A	20000314	US 1998-11347	19980511
PRIORITY APPLN. INFO.:			IT 1995-MI1560	19950719
			WO 1996-EP3201	19960719

AB Fluorogenic substrates susceptible of fluorescence emission and photosensitization by enzyme transformation suitable for diagnosis and photodynamic treatment of tumors are provided which consist of fluorescent substances with photosensitization activity, chem. modified with a group quenching the fluorescence and photosensitization properties, the said quencher group being removable by the cell enzyme activity with restoration of the properties of fluorescence and photosensitization activity of the original substance. Prepn. and testing of rose Bengal acetate rs included.

IT **11121-48-5**, Rose Bengal
RL: RCT (Reactant)
(modified fluorogenic substrates with enzyme-hydrolyzable quencher group for diagnosis and photodynamic treatment of tumors, and Rose Bengal acetate prepn.)

RN 11121-48-5 CAPLUS
CN Rose Bengal (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:43829 CAPLUS
DOCUMENT NUMBER: 126:154514
TITLE: Differential response of photosensitized young and old human erythrocytes to photodynamic activation
AUTHOR(S): Rollan, A.; McHale, A. P.
CORPORATE SOURCE: Biotechnology Research Group, School of Applied Biological and Chemical Sciences, University of Ulster, Coleraine Co. Londonderry, BT52 1SA, UK
SOURCE: Cancer Lett. (Shannon, Irel.) (1996), Volume Date 1997, 111(1,2), 207-213
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has recently been proposed that photosensitized erythrocytes may play an important role in the delivery and targeting of agents such as photosensitizers and chemotherapeutics for use in **cancer** treatment. It has been suggested that loading of photosensitized erythrocytes with chemotherapeutic agents would provide an ideal means of combining both treatment modalities. The recent application of real-time confocal laser scanning microscopy to the study of immediate effects of photodynamic activation on photosensitized erythrocytes has enabled us, in this study, to distinguish between the differential susceptibility of

age-d. resolved sub-populations of human erythrocytes to photodynamic activation. In this study we demonstrate that younger (low age-d.) sub-populations of photosensitized erythrocytes are less susceptible than older (high age-d.) sub-populations to photodynamic activation. We also demonstrate that this phenomenon is exhibited by cells photosensitized using hematoporphyrin deriv. and rose bengal as photosensitizers. In both cases no significant difference in uptake of photosensitizer by both populations could be obsd. using absorbance spectrophotometry. The study suggests that age-d. resoln. of erythrocytes prior to loading and photosensitization might provide a means of enhancing the release of loaded components from the photosensitized system and this would, in turn, enhance the potential use of photosensitized erythrocytes as delivery or targeting systems for use in combination **cancer** therapies.

IT **11121-48-5**, Rose bengal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photosensitizer; differential response of photosensitized young and old human erythrocytes to photodynamic activation with HPD or rose bengal and laser radiation)

RN 11121-48-5 CAPLUS
CN Rose Bengal (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

```
=> s gadolinium/cn

L5            1 GADOLINIUM/CN

=> d


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2000 ACS
RN   7440-54-2  REGISTRY
CN   Gadolinium (8CI, 9CI)  (CA INDEX NAME)
DR   87677-94-9, 110123-54-1
MF   Gd
CI   COM
LC   STN Files:   AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT,
       APIPAT2, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS,
       CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU,
       DETHERM*, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA,
ULIDAT,
       USPATFULL, VTB
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)


Gd


           18692 REFERENCES IN FILE CA (1967 TO DATE)
            2400 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           18721 REFERENCES IN FILE CAPLUS (1967 TO DATE)


=> s gadolinium iodide/cn

L6            1 GADOLINIUM IODIDE/CN

=> d


L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2000 ACS
RN   13572-98-0  REGISTRY
CN   Gadolinium iodide (GdI3) (6CI, 7CI, 8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Gadolinium iodide
CN   Gadolinium triiodide
MF   Gd I3
CI   COM
LC   STN Files:   CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, GMELIN*,
       IFICDB, IFIPAT, IFIUDB, MSDS-OHS, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
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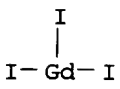

95 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
96 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

(FILE 'HOME' ENTERED AT 10:34:55 ON 10 AUG 2000)

FILE 'MEDLINE, SCISEARCH, EMBASE, USPATFULL' ENTERED AT 10:35:12 ON 10 AUG 2000

L1 34 S (HALOGEN? OR IODIN? OR BROMIN?) (3A) (XANTHENE?)
L2 29 DUP REM L1 (5 DUPLICATES REMOVED)
L3 77108 S (ROSE BENGAL) OR (TETRACHLOROTETRAIODOFLUORESCEIN) OR (?FLUOR
L4 5563 S L3 AND (RADIATION OR RADIO OR RADIOTHERAPY)
L5 4391 S L4 AND (TUMOR? OR CANCER? OR CELL? OR TISSUE?)
L6 6829 S (ROSE BENGAL) OR (TETRACHLOROTETRAIODOFLUORESCEIN)
L7 1030 S L6 AND L4
L8 654 S L7 AND L5
L9 619 DUP REM L8 (35 DUPLICATES REMOVED)
L10 0 S L2 AND (CANCER? OR TUMOR?)
L11 11 S L2 AND (CELL? OR TISSUE?)
L12 458 S L9 AND (?THERAP? OR TREAT?)
L13 458 DUP REM L12 (0 DUPLICATES REMOVED)
L14 90 S L12 AND ((PHLOXIN B) OR (ERYTHROSIN B) OR (EOSIN Y))
L15 0 S L12 AND ((PHLOXIN B) AND (ERYTHROSIN B) AND (EOSIN Y))
L16 654 S L6 AND L5
L17 362520 S (RADIATION OR RADIO? OR RADIOTHERAP?) (5P) (CANCER? OR TUMOR?
L18 4575 S L17 AND L3
L19 267506 S (TREAT? OR THERAP?) (3A) (CANCER? OR TUMOR? OR NEOPLASIA? OR
L20 1847 S L18 AND L19
L21 66 S L20 AND L6
L22 64 DUP REM L21 (2 DUPLICATES REMOVED)
L23 512 S L20 AND ((X-RAY) OR (ION? RADIATION))
L24 16 S L23 AND L6
L25 353543 S (CANCER OR TUMOR? OR NEOPLASIA?) (3A) (TREAT? OR ?THERAP?)
L26 0 S L25 AND L1
L27 1023 S L25 AND L4
L28 5 S L27 AND L14
L29 290 S L27 AND L23
L30 290 DUP REM L29 (0 DUPLICATES REMOVED)
L31 2 S L29 AND (CONTRAST MEDIA)
L32 162491 S (CANCER OR TUMOR? OR NEOPLASIA?) (A) (TREAT? OR ?THERAP?)
L33 185 S L30 AND L32
L34 185 S L33 AND L3
L35 3 S L33 AND L6
L36 39 S L32 AND (ROSE BENGAL)
L37 34 DUP REM L36 (5 DUPLICATES REMOVED)
L38 5268 S L32 AND ((ION? RADIATION) OR (X RAY?))
L39 10 S L38 AND L6
L40 10 S L38 AND (ROSE BENGAL)

L24 ANSWER 1 OF 16 USPATFULL
TI EGF-isoflavone conjugates for the prevention of restenosis

L24 ANSWER 2 OF 16 USPATFULL
TI Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

L24 ANSWER 3 OF 16 USPATFULL
TI Glutathione analogs as reagents

L24 ANSWER 4 OF 16 USPATFULL
TI Target-selective protocols based on mimics

L24 ANSWER 5 OF 16 USPATFULL
TI Glutathione analogs and paralog panels comprising glutathione mimics

L24 ANSWER 6 OF 16 USPATFULL
TI Use of secretory products of human lacrimal gland acinar epithelia for tear replacement therapy

L24 ANSWER 7 OF 16 USPATFULL
TI Treatment of ischemia/reperfusion injury with thalidomide alone or in combination with other therapies

L24 ANSWER 8 OF 16 USPATFULL
TI Peptide mediated enhancement of thrombolysis methods and compositions

L24 ANSWER 9 OF 16 USPATFULL
TI Glutathione analogs and paralog panels comprising glutathione mimics

L24 ANSWER 10 OF 16 USPATFULL
TI Method of inactivation of viral and bacterial blood contaminants

L24 ANSWER 11 OF 16 USPATFULL
TI Imidazole derivatives as protective agents in reperfusion injury and severe inflammatory responses

L24 ANSWER 12 OF 16 USPATFULL
TI Hydrogel compositions and methods of use

L24 ANSWER 13 OF 16 USPATFULL
TI Method of inactivation of viral and bacterial blood contaminants

L24 ANSWER 14 OF 16 USPATFULL
TI Vectored drug delivery system using a cephaloplastin linking agent and a
methed of using the system

L24 ANSWER 15 OF 16 USPATFULL
TI Conjugated polypeptides and methods for their preparation

L24 ANSWER 16 OF 16 USPATFULL
TI Method for the permanent occlusion of arteries

L14 ANSWER 1 OF 90 MEDLINE
TI Photocurable surgical **tissue** adhesive glues composed of photoreactive gelatin and poly(ethylene glycol) diacrylate.

L14 ANSWER 2 OF 90 USPATFULL
TI Apparatus for transport of fluids across, into or from biological **tissues**

L14 ANSWER 3 OF 90 USPATFULL
TI Optical fiber connector using photocurable adhesive

L14 ANSWER 4 OF 90 USPATFULL
TI Photopolymerizable biodegradable hydrogels as **tissue** contacting materials and controlled-release carriers

L14 ANSWER 5 OF 90 USPATFULL
TI Compliant **tissue** sealants

L14 ANSWER 6 OF 90 USPATFULL
TI Crosslinkable macromers bearing initiator groups

L14 ANSWER 7 OF 90 USPATFULL
TI Ternary photoinitiator system for curing of epoxy/polyol resin compositions

L14 ANSWER 8 OF 90 USPATFULL
TI Photopolymerizable biodegradable hydrogels as **tissue** contacting materials and controlled-release carriers

L14 ANSWER 9 OF 90 USPATFULL
TI Methods and compositions for enhancing the bioadhesive properties of polymers using organic excipients

L14 ANSWER 10 OF 90 USPATFULL
TI Compliant **tissue** sealants

(FILE 'HOME' ENTERED AT 12:27:37 ON 10 AUG 2000)

FILE 'MEDLINE, EMBASE, SCISEARCH, USPATFULL' ENTERED AT 12:28:06 ON 10 AUG 2000

L1 12101 S (CONTRAST? (2A) (MEDIA OR MEDIUM OR AGENT?)) AND ((X RAY?) OR

L2 14 S (HALOGEN? OR IODIN? OR BROMIN?) (W) (XANTHENE?)

L3 0 S L1 AND L2

L4 45 S L1 AND ((ROSE BENGAL) OR (TETRACHLOROTETRAIODOFLUORESCEIN) OR

L5 43 DUP REM L4 (2 DUPLICATES REMOVED)

L5 ANSWER 1 OF 43 USPATFULL
ACCESSION NUMBER: 2000:93135 USPATFULL
TITLE: Imaging of objects in turbid media based upon the preservation of polarized luminescence emitted from **contrast agents**
INVENTOR(S): Alfano, Robert R., 3777 Independence Ave., Bronx, NY, United States 10463
Demos, Stavros G., 32-72 30 St., Astoria, NY, United States 11106
Wang, Wubao, 138-10 Franklin Ave., Apt. 5B, Flushing, NY, United States 11355

	NUMBER	DATE	
PATENT INFORMATION:	US 6091983	20000718	
APPLICATION INFO.:	US 1997-797027	19970207	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-30054	19961106	(60)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Smith, Ruth S.
LEGAL REPRESENTATIVE: Kriegsman & Kriegsman
NUMBER OF CLAIMS: 41
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 1173

AB A method and system for imaging an object in a turbid medium. According to one embodiment, the method involves (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when appropriately excited with polarized radiation; (b) exciting the luminescent object through the turbid medium with polarized radiation so as to cause luminescent light to be emitted from the luminescent object, the luminescent light initially being at least partially polarized; (c) after the luminescent light has emerged from the turbid medium, the luminescent light consisting of a ballistic component, a snake-like component and a diffuse component, detecting a pair of complementary polarization components of the luminescent light; and (d) forming an image of the object using the pair of complementary polarization components.

TI Imaging of objects in turbid media based upon the preservation of polarized luminescence emitted from **contrast agents**

AB . . . turbid medium. According to one embodiment, the method involves (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when appropriately excited with polarized radiation; (b) exciting the luminescent. . .

SUMM . . . medium is highly desirable. For instance, the detection of a tumor embedded within a tissue is one such example. Although **X**-**ray** techniques do provide some measure of success in detecting objects in turbid media, they are not typically well-suited for detecting. . . e.g., tumors less than 1 mm in size embedded in tissues, or for detecting objects in thick media. In addition, **X**-**ray** radiation can present safety hazards to a person exposed thereto. Ultrasound and magnetic resonance imaging (MRI) offer

alternatives to the use of **X-rays** but have their own drawbacks.

SUMM . . . transillumination imaging technique wherein an object hidden in a scattering medium is made luminescent by the addition thereto of a **contrast agent**, and luminescent light emitted from the **contrast agent** is selected for imaging while the illuminating light is filtered out. The technique is based in part on the observation. . . be further improved by introducing an absorbing dye into the turbid medium that preferentially absorbs the luminescent light from the **contrast agent**. In this manner, because the multiply scattered light travels over a longer path length than the ballistic signal, the multiply. . .

SUMM In addition to being used in the aforementioned manner, **contrast agents** have also been used in connection with a variety of different medical imaging techniques (e.g., **X-ray**, PGT, and CAT tomography) to enhance image quality and to increase the quantity of information obtained. The polarization properties of fluorescent light emitted by several **contrast agents**, such as **Eosin**, Rose Begal and TCTIF in non-turbid media, have been studied using picosecond time-dependent fluorescence measurements. See Fleming et al., "Direct. . . Lett., 49:416-20 (1977), both of which are incorporated herein by reference. The results of such studies show that the aforementioned **contrast agents**, when photoexcited by polarized light, emit partially polarized light, keeping the preferred polarization of the pump light.

SUMM . . . the diffuse component of polarized light becomes randomly polarized as it travels through a turbid medium and (2) that certain **contrast agents** emit at least partially polarized luminescent light when photoexcited with polarized light, the partially polarized luminescent light keeping the preferred. . .

SUMM . . . a turbid medium, said method comprising the steps of: (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when appropriately excited; (b) exciting the luminescent object through the. . .

SUMM The **contrast agent** of the present invention, instead of being of the type that emits at least partially polarized luminescent light upon illumination. . . emits polarized luminescent light regardless of whether the illuminating light is polarized. In the case of said latter type of **contrast agent**, the present invention relates to a method for imaging an object located in a turbid medium, said method comprising the steps of: (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits polarized light when appropriately excited; (b) exciting the luminescent object through the turbid medium with. . .

DRWD . . . 2(a) through 2(c) are images obtained using the system of FIG. 1 of a 1-mm pipette filled with a luminescent **contrast agent** and positioned within a quantity of 0.08% intralipid solution, the images being formed of (a) the parallel component of the. . .

DRWD . . . 3(a) through 3(c) are images obtained using the system of FIG. 1 of a 1-mm pipette filled with a luminescent **contrast agent** and positioned within a quantity of 0.08% intralipid solution and Malachite Green absorbing dye, the images being formed of (a). . .

DRWD . . . 5(a) through 5(c) are images obtained using the system of FIG. 1 of a 1-mm pipette filled with a luminescent **contrast agent** and positioned within a quantity of 0.09% intralipid solution, the images being formed of (a) the parallel component of the. . .

DRWD FIG. 18 is a graphic representation of the parallel and perpendicular components of the luminescence, over time, of the **contrast agent** Cardio Green in water following 630 nm excitation;

DETD . . . diffuse component of initially polarized light loses its

polarization as it travels through a turbid medium; and (2) that certain **contrast agents** emit at least partially polarized luminescent light when photoexcited with pump light, some of said **contrast agents** emitting polarized luminescent light regardless of whether the pump light is polarized, other of said **contrast agents** emitting partially polarized luminescent light only when the pump light is polarized, the partially polarized luminescent light keeping the preferred. . .

DETD . . . a first embodiment, said method comprises the steps of (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when excited with polarized radiation; (b) exciting the luminescent object. . .

DETD The illuminating polarized radiation can be in the form of pulsed or continuous wave light (lamp or laser), **X-rays** or particle beam. Preferably, the illuminating polarized radiation is either continuous wave or pulsed light. Preferably, the illuminating polarized light. . .

DETD . . . a second embodiment, said method comprises the steps of (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits polarized light when excited; (b) exciting the luminescent object through the turbid medium with radiation,. . .

DETD . . . is a 1-mm diameter pipette 21. Pipette 21, which is disposed along the path of beam 14, is filled with **Eosin**, a **contrast agent**, at a concentration of 1.times.10.sup.-4 M diluted in C.sub.2 H.sub.5 OH. **Eosin** strongly absorbs at 532 nm and emits in the 570-640 nm spectral region with an emission peak at 580 nm. When illuminated with linearly polarized light, **Eosin** emits light that is partially polarized, the ratio between the parallel and perpendicular polarization components being approximately 1.2 to 1,. . .

DETD . . . 25. Notch filter 27 is used to cut off the illuminating light so that only the luminescent emission from the **contrast agent** is recorded by CCD camera 23, and polarizer 29 is set in one direction (y-axis) so as to selectively pass. . .

DETD . . . 14 travel through the turbid medium of glass cell 19 and reach pipette 21, they are still partially polarized. The **contrast agent** within pipette 21 absorbs the partially polarized light and emits light photons which are also partially polarized. The polarized portion. . .

DETD . . . solution in glass cell 19 was chosen so that only a very small portion of the light emitted by the **contrast agent** within pipette 21 would not undergo scattering. Those photons that did not undergo scattering, i.e., the ballistic photons, contributed to. . . line in the middle of the image shown in FIGS. 2(a) and 2(b), which is a direct image of the **contrast agent**-containing pipette. In FIG. 2(c), the direct image of the pipette is enhanced with respect to the intensity of the rest. . .

DETD . . . luminescent light. To determine if a similar improvement could be obtained in connection with the present method, we introduced the **contrast agent** Malachite Green to the scattering medium and obtained images of the parallel component (FIG. 3(a)), the perpendicular component (FIG. 3(b)). . .

DETD . . . now to FIGS. 5(a) through 5(c), there are shown images obtained using the system of FIG. 1 of the same **Eosin**-filled pipette now positioned within a quantity of 0.09% intralipid solution, the images being formed of (a) the parallel component of. . . respectively. With the concentration of the intralipid solution set at 0.09%, virtually none of the ballistic photons emitted from the **contrast agent** reach the detector. As can be seen, the parallel and perpendicular component images of FIGS. 5(a) and 5(b), respectively, differ. . .

DETD . . . behind the invention, the present inventors believe that this improvement in image quality can be explained as follows: (1) the **contrast agent Eosin** emits partially polarized luminescent light; and (2) the subtraction of the perpendicular component from the parallel component substantially eliminates the. . .

DETD . . . at least partially polarized. This requirement can be achieved by making the object luminescent by the addition thereto of a **contrast agent** of the type that emits partially polarized light when photoexcited with polarized light. **Eosin**, Rose Begal and TCTIF, Cardio Green, photofrin, HPD and porphyrin derivative dyes are examples of such a **contrast agent** . Other such **contrast agents** include certain dyes, phosphors, dielectrics, ceramics, semiconductors, and impurity doped materials, such as Eu-doped and Cr-doped powders. Preferably, the **contrast agent** emits optical radiation in the spectral region between 400 and 1600 nm. In addition, where the present technique is used to image diseased tissues, the **contrast agent** preferably exhibits an affinity for such diseased tissues (e.g., cancerous tissues).

DETD . . . that the object emit at least partially polarized light can be met by the addition to the object of a **contrast agent** of the type that emits polarized light when photoexcited, regardless of whether the photoexciting light is itself polarized. Still another. . . way in which this requirement can be met is by selecting an object that, even without the use of a **contrast agent**, inherently emits at least partially polarized luminescent light when photoexcited. For any of the above alternatives, the luminescent object preferably. . .

DETD . . . many applications, one such application being medical imaging. For example, as alluded to above, by administering to a patient a **contrast agent** that preferentially bind to cancerous tumors and that also emits at least partially polarized luminescent light when appropriately photoexcited (e.g.,. . .

DETD . . . passed through polarizer 305 is then used to illuminate the tissue in question, i.e., a gland to which a luminescent **contrast agent** that preferentially binds to cancerous or precancerous tissue has previously been added. System 301 additionally includes an analyzer 307 through. . .

DETD . . . is used to direct the illuminating light from fiber 357 onto the prostate tissue being examined (to which a luminescent **contrast agent** that preferentially binds to cancerous or precancerous tissue has previously been added) and to direct the light emitted from the. . .

DETD . . . the present invention may be useful in medical imaging, especially when the backscattering geometry is used for subsurface imaging. The **contrast agents** to be used for medical imaging have all the properties discussed above and, in addition, bind to molecules associated and/or involved in tumors, cancers, brain disorders, liver disorders or other disorders or diseases of the human body. Such **contrast agents**, when injected into the human body, will concentrate themselves primarily in the diseased parts of the human body; therefore, using. . .

DETD By practicing the present technique in a backscattering geometry, one can examine the emission from a **contrast agent** associated with a disease located in the glands under the arm, such as for breast cancer screening. The backscattering geometry. . . the prostate by inserting an appropriate imaging probe in the rectum. Photoactive drugs could be tailored to be used as **contrast agents** for a wide range of diseases, the drugs being capable of being absorbed by diseased tissues and emitting light in. . .

DETD We have tested the above concepts in tissues using the dye Cardio Green as the **contrast agent**. Cardio Green exhibits strong absorption in the 720-820 nm spectral region and emits in the 800-860 nm

spectral region. The. . .

CLM What is claimed is:

. . . a turbid medium, said method comprising the steps of: (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when appropriately excited with polarized radiation; (b) exciting the luminescent. . .

. . . as claimed in claim 1 wherein the exciting polarized radiation is selected from the group consisting of exciting polarized light, **X-rays** and particle beam.

16. The method as claimed in claim 1 wherein said **contrast agent** is selected from the group consisting of dyes, phosphors, dielectrics, ceramics, semiconductors and impurity-doped materials.

17. The method as claimed in claim 16 wherein said **contrast agent** is selected from the group consisting of **Eosin**, Rose Begal, Cardio Green, photofrin, HPD, porphyrin derivative dyes and TCTIF.

18. The method as claimed in claim 1 wherein said **contrast agent** is **Eosin**.

19. The method as claimed in claim 1 wherein said **contrast agent**, when excited, emits at least partially polarized light with an optical relaxation time in the range of 50 ps to. . .

20. The method as claimed in claim 1 wherein said **contrast agent**, when excited, emits light in the spectral region between 400 and 1600 nm.

21. The method as claimed in claim 1 wherein the turbid medium is a tissue and wherein said **contrast agent**, when excited, emits light in the absorption range of the tissue.

22. The method as claimed in claim 1 wherein the turbid medium is a tissue and wherein said **contrast agent** preferentially binds to malignant, as opposed to non-malignant, tissue.

23. The method as claimed in claim 1 wherein the **contrast agent** is of the type that preferentially binds to molecules associated with cancers, disorders or diseases of the human body.

. . . a turbid medium, said method comprising the steps of: (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits at least partially polarized light when appropriately excited with polarized radiation; (b) exciting the luminescent. . .

. . . a turbid medium, said method comprising the steps of: (a) making the object luminescent by adding to the object a **contrast agent** of the type that emits polarized light when appropriately excited; (b) exciting the luminescent object through the turbid medium with. . .

. . . 33. The method as claimed in claim 28, wherein the exciting radiation is selected from the group consisting of light, **X-rays** and particle beam.

37. The method as claimed in claim 28, wherein the **contrast agent** emits linearly polarized luminescent light and wherein said pair of complementary polarization components are parallel and perpendicular to the linearly. . .

41. The method as claimed in claim wherein 40 wherein the **contrast agent** is of the type that preferentially binds to molecules associated with cancers, disorders or diseases of the human body.

L5 ANSWER 7 OF 43 USPATFULL

ACCESSION NUMBER:	2000:37781 USPATFULL
TITLE:	Diagnosis and treatment of arterial chlamydial granuloma
INVENTOR(S):	Shor, Allan, 76 Klip Street, Observatory Extension, Johannesburg 2000, South Africa Kuo, Cho-chou, Seattle, WA, United States
PATENT ASSIGNEE(S):	Board of Regents of the University of Washington, Seattle, WA, United States (U.S. corporation) Shor, Allan, Johannesburg, South Africa (non-U.S. individual)

	NUMBER	DATE
PATENT INFORMATION:	US 6043225	20000328
APPLICATION INFO.:	US 1998-6089	19980113 (9)

RELATED APPLN. INFO.:	Division of Ser. No. US 1995-452652, filed on 25 May 1995, now patented, Pat. No. US 5830874 which is a division of Ser. No. US 1992-898905, filed on 12 Jun 1992, now patented, Pat. No. US 5424187
DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Cook, Rebecca
LEGAL REPRESENTATIVE:	Christensen O'Connor Johnson & Kindness PLLC
NUMBER OF CLAIMS:	12
EXEMPLARY CLAIM:	11
NUMBER OF DRAWINGS:	20 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT:	2070

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method of diagnosing arterial chlamydial granuloma by detecting in a biological sample both a first marker associated with Chlamydia pneumoniae and a second marker associated with arterial granuloma. Therapeutic composition for treating arterial chlamydial granulomatous disease, including an anti-Chlamydia pneumoniae agent and a granuloma inhibitor.

DETD . . . disease. Sites of infection with the TWAR organism may be identified, e.g., in serial histological sections stained with hematoxylin and **eosin**, by identifying sections containing a focal macrophage infiltrate and verifying the presence of the TWAR organism in macrophages, smooth muscle. . .

DETD . . . arterial granulomatous disease that are associated with arterial lumen narrowing. Lumenal obstruction is commonly detected by angiographic methods using an **X-ray** opaque dye that is frequently introduced with a catheter into the artery of interest. Pursuant to the present disclosure, it is highly desirable in such a catheter protocol to introduce a diagnostic imaging agent either along with the **contrast agent** or shortly thereafter. For instance, a .sup.99m Tc-labeled anti-Chlamydia specific binding partner (or NMR-labeled specific binding partner) may be used. . . In this manner patients that have arterial chlamydial infection can be identified by the coincidence of lumenal narrowing (e.g., in **X-ray**) and chlamydial marker (e.g., in a gamma camera image of the same site). An illustrative example of a diagnostic imaging. . .

DETD Procedure: Catheter procedures designed for angiography are also suitable for delivery of both an **X-ray** opaque **contrast agent** and a diagnostic Chlamydia-specific imaging agent. Briefly, the catheter is threaded into the artery and placed upstream of the blockage, and the **contrast**

agent and radiolabeled monoclonal antibody are either delivered together, or one after the other. After a suitable time the luminal narrowing is detected by **X-ray** techniques, and the presence of the radiolabeled imaging agent is detected at the same site using a gamma camera, or,. . .

L5 ANSWER 30 OF 43 USPATFULL
ACCESSION NUMBER: 91:37551 USPATFULL
TITLE: Method and apparatus for high resolution holographic imaging of biological tissue
INVENTOR(S): Bjelkhagen, Hans, Chicago, IL, United States
Friedman, Marc D., Watertown, MA, United States
PATENT ASSIGNEE(S): Biologic Systems Corp., Mundelein, IL, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5014709	19910514	
APPLICATION INFO.:	US 1989-365336	19890613	(7)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Smith, Ruth S.
LEGAL REPRESENTATIVE: Welsh & Katz, Ltd.
NUMBER OF CLAIMS: 78
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 678

AB Apparatus and methods for high resolution holographic recordation and microscopic examination of the holographic image of biological tissue. A single beam Denisyuk holographic recordation of the biological tissue is obtained with direct contact or close proximity to the tissue. Contrast enhancement by staining with a dye selected to maximize absorption of the light frequency used to record the hologram is used to improve contrast and resolution. A liquid interface is formed between the recording film and the subject tissue to improve image quality and resolution. The resulting high resolution three dimensional holographic images may be examined under microscope magnification for such applications as medical biopsy.

SUMM . . . still photography techniques which have limited resolution and which only provide 2-dimensional visualization of the desired structures. Another method employs **x-ray** scanning, but this also has low resolution, the equipment is expensive to purchase and maintain, and radiation exposure may prove. . .

DETD . . . surface tissue. Thus, in-vivo holograms of live tissue may be obtained. A tube 28 may be provided to channel a **contrast** enhancing **medium**, such as a dye or powder from a reservoir 27 to the placement device 22 to permit contrast enhancement (e.g.,. . .

DETD . . . methylene blue, or toluidine blue o provide strong red absorption in combination with a Krypton laser, and (2) phloxine b, **rose bengal**, new fuchsin provide strong green absorption in combination with an Argon laser. These dyes, which have been approved by the. . .

DETD . . . (DMSO) may be used to penetrate into the tissue. Optionally, a dye may be injected below the surface, or a **contrast** enhancing **agent** may be injected into the blood stream and absorbed by the subject tissue. To enhance blood vessels, etc., a **contrast** enhancing **agent** can simply be injected into the blood stream enabling three dimensional images of the blood vessels, capillaries, etc. In addition,. . .

CLM What is claimed is:
43. The method of claim 26 wherein the step of contrast enhancing comprises injecting a **contrast** enhancing **medium** to

enhance features of the biological tissue.

L6 ANSWER 4 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998271862 EMBASE
TITLE: High sensitivity of Deinococcus radiodurans to photodynamically-produced singlet oxygen.
AUTHOR: Schafer M.; Schmitz C.; Horneck G.
CORPORATE SOURCE: M. Schafer, DLR, Institute Aerospace Medicine, Linder Hohe, D51170 Koln, Germany
SOURCE: International Journal of Radiation Biology, (1998) 74/2 (249-253).
Refs: 18
ISSN: 0955-3002 CODEN: IJRBA3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 014 Radiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose: To study the sensitivity of two bacterial cell systems to photodynamic treatment and X-ray irradiation as part of a project to establish efficient procedures for waste water disinfection. Materials and methods: Stationary-phase cells of Deinococcus radiodurans (Gram-positive) and Escherichia coli (Gram-negative) were exposed to visible light in a buffer solution containing up to 5 .mu.g/ml sensitizer **rose bengal** (RB) and to X-rays at dose rates of 32.8 Gy/min or 14.6 Gy/min, respectively. Results: Survival of both cell types decreased with increasing exposure time to visible light and increasing concentration of RB, and therefore with an increase in singlet oxygen production. Surprisingly, D. radiodurans, the most resistant cell system to **ionizing radiation**, was more sensitive to photodynamic treatment than E. coli by about a factor of 100. Conclusions: The main target of singlet oxygen reaction is the cell membrane. The repair of such damage in D. radiodurans is less effective than in E. coli.

L6 ANSWER 5 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95296614 EMBASE
DOCUMENT NUMBER: 1995296614
TITLE: Photodynamic and radiolytic inactivation of ion channels formed by gramicidin A: Oxidation and fragmentation.
AUTHOR: Kunz L.; Zeidler U.; Haegele K.; Przybylski M.; Stark G.
CORPORATE SOURCE: Fakultat fur Biologie, Universitat Konstanz, Postfach 5560 M638,D-78434 Konstanz, Germany
SOURCE: Biochemistry, (1995) 34/37 (11895-11903).
ISSN: 0006-2960 CODEN: BICHAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ion channels formed by the peptide gramicidin A in planar lipid membranes have been reported to react very sensitively upon irradiation of the membrane by **ionizing radiation** (radiolysis), by UV light (photolysis), or by visible light in the presence of appropriate photosensitizers (photodynamic inactivation). In all three cases the effect is due to the presence of the four tryptophan residues of the pentadecapeptide. Modifications of these amino acids-due to an interaction

with free radicals formed upon water radiolysis or due to light absorption-have been found to reduce the membrane conductance by many orders of magnitude. The present study was intended to correlate functional changes, observed at the level of single ion channels, with changes of the molecular structure identified by mass spectrometry. About 98% of the inactivated channels showed a single-channel conductance of virtually zero, while about 2% of the channels present before irradiation are converted to a state of reduced conductance (and reduced lifetime). On the structural level, irradiation in the presence of the photosensitizer **Rose Bengal** was found to produce oxidation and fragmentation of the peptide at the positions of the tryptophan residues. Our results provide evidence that the main effect of radiolysis, or of photodynamic treatment, is the cleavage of the peptide backbone leading to immediate closure of an open ion channel.

L9 ANSWER 7 OF 27 MEDLINE
TI **Iodine**-123-**Rose bengal**: An improved hepatobiliary imaging agent.

L9 ANSWER 8 OF 27 MEDLINE
TI [Studies of the **radiation** reactions of the liver using the **iodine** 131-**rose bengal** test].
Untersuchungen der Strahlenreaktionen der Leber mit Hilfe des Jod 131-Bengalrosatestes.

L9 ANSWER 9 OF 27 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI Liberation of halide ions from xanthene colors (Food Red Nos. 3, 104 and 105) by photo-irradiation.

L9 ANSWER 19 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
TI **IODINE**-131 **ROSE BENGAL** THERAPY IN HEPATOBLASTOMA PATIENTS.

L9 ANSWER 20 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
TI EXPERIMENTAL AND CLINICAL ASSESSMENT OF **IODINE** 123 **ROSE BENGAL**.

L9 ANSWER 21 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
TI HEPATOSCINTIGRAPHY USING **IODINE**-123-LABELED **ROSE BENGAL**.

L9 ANSWER 22 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
TI COMPARISON OF **IODINE**-131 LABELED **ROSE BENGAL** CLEARANCE SENSITIVITY FROM THE RESULTS OF DIGITAL PROCESSING OF THE DATA ON EXTERNAL COUNT.

L9 ANSWER 7 OF 27 MEDLINE
ACCESSION NUMBER: 75213088 MEDLINE
DOCUMENT NUMBER: 75213088
TITLE: **Iodine**-123-**Rose bengal**: An improved hepatobiliary imaging agent.
AUTHOR: Serafini A N; Smoak W M; Hupf H B; Beaver J E; Holder 4; Gilson A J
SOURCE: JOURNAL OF NUCLEAR MEDICINE, (1975 Jul) 16 (7) 629-32. Journal code: JEC. ISSN: 0161-5505.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197512

AB A practical method for preparing)23-I-rose bengal that allows for its rapid and efficient incorporation into the molecule is reported. Administration of 123-I-rose bengal to normal healthy patients showing the normal uptake and excretory pattern visualized with this radio pharmaceutical is also presented. The overall reduction in imaging time and **radiation** exposure together with the improved images possible should greatly improve our diagnostic capabilities in evaluating the jaundiced patient.

L9 ANSWER 19 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1991:343700 BIOSIS
DOCUMENT NUMBER: BA92:43075
TITLE: **IODINE**-131 **ROSE BENGAL** THERAPY IN HEPATOBLASTOMA PATIENTS.
AUTHOR(S): DE KRAKER J; HOEFNAGEL C A; VOUTE P A
CORPORATE SOURCE: WERKGROEP KINDERTUMOREN, EMMA KINDERZIEKENHUIS/HET KINDER AMC, MEIBERGDREEF 9, NL-1105 AZ AMSTERDAM, NETHERLANDS.
SOURCE: EUR J CANCER, (1991) 27 (5), 613-615.
CODEN: EJCAEL. ISSN: 0959-8049.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB If conventional treatment modalities have failed in hepatoblastoma patients and no distant metastases can be demonstrated therapy with radionuclide agents can be considered. In 6 patients diagnostic technetium-99m (99mTc)-disofenin and two **iodine**-131 (131I)-**rose bengal** scans were made. 2 patients demonstrated specific uptake of disofenin. One of these had a positive scintigram with radiolabelled **rose bengal**. This patient was subsequently treated with 1.1 GBq 131I-**rose bengal**. No toxicity was observed. A clear decrease in the level of alpha-fetoprotein indicated a response and demonstrated that this radiopharmaceutical can be used for tumour targeted **radiation** therapy in selected patients with therapy resistant tumours.

ANSWER 21 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:307297 BIOSIS
DOCUMENT NUMBER: BA90:26264
TITLE: HEPATOSCINTIGRAPHY USING **IODINE**-123-LABELED **ROSE BENGAL**.
AUTHOR(S): VOLKOV A A; KOMAROV E I; KOZLOV A A; BYKOV S A; ARTYUSHKIN A V; SKUDRIT G V; YAKOVLEVA L A; MOROZOVA O M; OSIPOV I S; ET AL
CORPORATE SOURCE: CENT. RES. ROENTGENOL.-RADIOL. INST., MINIST. HEALTH USSR, LENINGRAD, USSR.
SOURCE: MED RADIOL, (1989) 34 (12), 14-18.
CODEN: MERAA9. ISSN: 0025-8334.
FILE SEGMENT: BA; OLD
LANGUAGE: Russian

AB The paper is devoted to the experience in diagnostic investigations using rose bengal, labeled with half-life 123I (123I-RB). The drug was synthesized in the B. P. Konstantinov Leningrad Institute of Nuclear Physics, USSR Academy of Sciences. Analysis of the results of investigations of 201 patients with diseases of the liver and biliary tracts revealed with diseases of the liver and biliary tracts revealed the advantages of 123I-RB over standard RPs of similar diagnostic purpose. Owing to low **radiation** exposure one could use higher activity (up to 120 MBq and more) of the drug. It made it possible to combine a study of the functional parameters of the hepatobiliary system and obtaining scintigraphic data on the structure of the liver and biliary tracts. 123I-RB is the best radiodiagnostic agent for a study of function and topography of the liver in patients with an increased blood level of bilirubin.

L9 ANSWER 22 OF 27 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1980:241103 BIOSIS
DOCUMENT NUMBER: BA70:33599
TITLE: COMPARISON OF **IODINE**-131 LABELED **ROSE** **BENGAL** CLEARANCE SENSITIVITY FROM THE RESULTS OF DIGITAL PROCESSING OF THE DATA ON EXTERNAL COUNT.
AUTHOR(S): EL'DARKHANOVA P YU; SMIRNOV V F
CORPORATE SOURCE: CENT. INST. POSTGRAD. MED., MOSCOW, USSR.
SOURCE: MED RADIOL, (1979) 24 (9), 25-31.
CODEN: MERAA9. ISSN: 0025-8334.
FILE SEGMENT: BA; OLD
LANGUAGE: Russian

AB An algorithm for determining parameters of the bioexponential function approximating the external count of **radiation** was used to find a number of indices of the blood clearance of 131I-Bengal rose. With data processing a control group and patients with duodenal ulcer, enterocolitis, pulmonary tuberculosis and chronic hepatitis were investigated. The most sensitive indices for detecting small shifts in the excretory function of hepatites are the time constant .lambda.1 of the last exponential compound of the recorded signal and the K12 coefficient of indicator transfer from the plasma to the liver corresponding to a reversible double-chamber model of Bengal rose distribution. To determine this index record **radiation** above the temporal region for 30 min after administration of 0.2 .mu.Ci of the isotope/1 kg body wt.

L10 ANSWER 10 OF 13 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 94:515050 SCISEARCH
THE GENUINE ARTICLE: PB526
TITLE: EFFECTS OF COMPLEXATION BY CYCLODEXTRINS ALPHA-CYCLODEXTRIN CYCLOMALTOHEXAOSE, BETA-CYCLODEXTRIN CYCLOMALTOHEPTAOSE GAMMA-CYCLODEXTRIN CYCLOMALTOOCTAOSE ON THE PHOTOREACTIVITY OF ROSE-BENGAL AND ERTHROSIN-B - A LASER FLASH-PHOTOLYSIS INVESTIGATION
AUTHOR: FLAMIGNI L (Reprint)
CORPORATE SOURCE: CNR, IST FRAE, VIA P GOBETTI 101, I-40129 BOLOGNA, ITALY (Reprint)
COUNTRY OF AUTHOR: ITALY
SOURCE: JOURNAL OF THE CHEMICAL SOCIETY-FARADAY TRANSACTIONS, (21 AUG 1994) Vol. 90, No. 16, pp. 2331-2336.
ISSN: 0956-5000.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: ENGLISH
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The effect of complexation by cyclodextrins on the photoreactivity of the **halogenated xanthenes** Rose Bengal and Erythrosin 8 has been studied by detecting the change induced in the yield and reactivity of triplet and radical states. Solutions of Rose Bengal and Erythrosin B in gamma-cyclodextrins, containing 90% of complex in the ground state, and solutions of erythrosin B in alpha-cyclodextrins, containing 60% of complex in the ground state, were studied by laser flash photolysis. Other complexes could not be prepared in useful fractions, either because of the low solubility of the complexing cyclodextrin or because of the low values of the association constants. The spectrum and the yield of triplet and radical intermediates appear to be identical in water and in systems containing the complexed form. The rates of reaction of the triplets and radicals in the complexed system are slower than in water. The exit rate constant of triplet is less than 2 x 10(5) s-1 and the inclusion complex of triplet and radicals has an equilibrium constant similar to that of the ground state. A stoichiometry ratio of 1 : 1 was confirmed for all complexes, but there is an indication of some contribution from 2 : 1 (host : guest) in the gamma cyclodextrin-erythrosin 8 system.

(FILE 'HOME' ENTERED AT 09:14:32 ON 12 MAR 2001)

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, USPATFULL' ENTERED AT 09:17:54 ON 12 MAR 2001

L1 830 S (CANCER? OR TUMOR?) AND (XANTHENE? OR (ROSE BENGAL))
L2 416 S L1 AND (RADIATION OR RADIO?)
L3 390 DUP REM L2 (26 DUPLICATES REMOVED)
L4 0 S L3 AND (HALOGEN? (3A) XANTHENE)
L5 235 S L3 AND (ROSE BENGAL)
L6 1 S L5 AND ((ROSE BENGAL) (5A) TREAT? (5A) (CANCER? OR TUMOR?))
L7 1 S L5 AND ((ROSE BENGAL) (10A) TREAT? (10A) (CANCER? OR TUMOR?)
L8 0 S L5 AND ((ROSE BENGAL) (10A) TREAT? (10A) (CANCER? OR TUMOUR?